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## SPECIAL ARTICLE.

### THE HUXLEY LECTURE ON RECENT STUDIES OF IMMUNITY, WITH SPECIAL REFERENCE TO THEIR BEARING ON PATHOLOGY.*

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You will readily believe that with my deep appreciation of the high honor conferred by the invitation to deliver the fourth Huxley lecture there was joined a sense of great embarrassment in being called upon to follow in this office three such leaders of world-wide fame as Sir Michael Foster, Professor Virchow and Lord Lister. But the letter of the Committee of Charing Cross Hospital Medical School stated that the choice of a successor to these great names was "a tribute of our admiration for the great army of scientific workers on the other side of the Atlantic." While I cannot assume to occupy any other place in this army than that of a soldier in the ranks, I felt that if my acceptance of this invitation could be regarded as in any sense an expression of appreciation by American workers in science of the commendation and goodwill of their British colleagues, of our large indebtedness to them, of our sense of the common interests, the comradeship and the kinship of the English-speaking peoples on both sides of the ocean, I should not decline, even if summoned to occupy a position of danger.

There was another consideration which I may be permitted here to mention. Through Huxley there is, if not a bond, at least a link between the Charing Cross Hospital Medical School and the Johns Hopkins University. This lectureship was founded to commemorate the fact that Huxley received his entire medical education at the Charing Cross Hospital Medical School. While throughout America the name of Huxley is held in high honor as that of a great discoverer and interpreter in science, and while the influence which he has exerted upon popular as well as scientific opinion through those messages peculiarly fitted to the needs of English thought is not less here than among his own countrymen, we at the Johns Hopkins University have special reasons to acknowledge our gratitude to him. He crossed the ocean to deliver the principal address at the opening of this University in 1876, and he then gave utterance to ideas concerning university, and especially medical, education which were at the time and have remained an inspiration and a guide to us. Then, too, the Johns Hopkins University owes to Huxley and to Michael Foster the accession to its faculty of my lamented colleague, Newell Martin, who by the introduction and development of the biological methods and conceptions of his teachers gave such new directions and so great an impulse to biological study in America that his own work and that of his pupils started for us a new era in this department.

The first Huxley lecturer has made it unnecessary for his successors to dwell upon Huxley's studentship at the Charing Cross Hospital, upon the important influence which this had upon his career, or upon his great services to medical science, although his chief title to fame lies outside of the domain of medicine. I should like, however, to quote a passage, although it must be familiar to you, from Mr. Leonard Huxley's charming "Life and Letters" of his father, which has appeared since the date of Sir Michael Foster's lecture, for it shows that "it was at Charing Cross Hospital where Huxley first felt the influence of daily intercourse with a really able teacher." He says: "No doubt it was very largely my own fault, but the only instruction from which I obtained the proper effect of education was that which I received from Mr. Wharton Jones, who was the lecturer on physiology at the Charing Cross School of Medicine. The extent and precision of his knowledge impressed me greatly, and the severe exactness of his method of lecturing was quite to my taste. I do not know that I have ever felt so much respect for anybody as a teacher before or since." Wharton Jones, who will doubtless be longest remembered as the discoverer of the ameboid movements of the white blood corpuscles, was an experimental physiologist and pathologist of much originality, and it seems to me that there has not been, even in his own country, so full a recognition of his work as its importance merits.

Before passing to the special theme of this lecture it is fitting that I should pause, if only for a moment, to call to mind with affection and reverence that recently departed great man who honored and delighted you four years ago, and who has conferred such high distinction upon the office of Huxley lecturer. When one considers the full import of the discovery and establishment by Virchow of the principles of cellular pathology, that this constitutes the secure foundation upon which nearly two generations have built and future generations will continue to build the edifice of scientific medicine, I do not know what greater name there is in the whole history of medicine than that of Rudolf Virchow. How noble his character! With what amazing industry, versatility and keenness of intellect did he fruitfully cultivate the new fields which he had opened to research, as well as other departments of science! With what devotion and bene-

*Delivered at the opening of the Winter Session of Charing Cross Hospital Medical School, October 1, 1902.

ficial results did he give his time and abundant knowledge to the service of the public and of our profession! We mourn the loss of a hero of medicine and of science, a benefactor of his race, and we rejoice in the rich fruitage of a long and well-spent life.

The first place in experimental medicine to-day is occupied by the problems of immunity, and in accordance with the trust of the Huxley Lectureship, which provides that the lecture shall relate to "recent advances in science and their bearing upon medicine and surgery," I have chosen for my theme "Recent Studies of Immunity, with Special Reference to their Bearing on Pathology." As it would be hopeless to attempt a complete review of this broad subject within the space of a single lecture, I shall dwell more particularly upon certain of its aspects, not always of necessity the most important ones, which I conceive less familiar to most physicians, or which have engaged my attention, although much which I shall say is, of course, known to those who have followed the results of recent work in these new lines of investigation.

Under "Studies of Immunity" I have included, as a matter of convenience, though not with strict accuracy, investigations which, although the direct outgrowth of those primarily directed towards a solution of the problems of immunity, have extended far beyond these bounds, and have revealed specific properties of cells and fluids in health and disease of the broadest biological interest. We find illustrated here the familiar fact, nowhere more important to recognize than in medicine, that the sciences are interdependent, that discovery in one field sheds light in the most diverse and often unexpected directions, and opens new paths to research. We shall see also exemplified the fructifying influence upon the advancement of knowledge of the discovery and application of new methods of investigation.

In endeavoring to follow in its intimate workings the contest of the living body with its invaders, the attention of investigators has naturally been drawn both to the action of the cells and to the properties of the fluids of the body in this struggle, to the latter sometimes without sufficient consideration of the dependence of the humors in their composition upon the cells. Each of these lines of study, whether followed separately or conjointly, has led to the discovery of important facts relating to the mechanism of immunity.

We owe to Metchnikoff and his pupils the most important observations concerning the direct participation of leucocytes and other cells in the processes of infection and the production of immunity. Whatever attitude one may take toward Metchnikoff's well-known phagocytic theory of immunity, one must recognize the wealth of new facts which he has brought to light, and must admire the skill and fertility of resource with which for two decades he has defended this theory against severe assaults; and he has done so, in my judgment, with a large measure of success. With wonderful ingenuity in his recent book on "Immunity" he rescues the phagocytes and applies to a deeper insight into their activities results of his opponents' work.

The other line of research, in some respects more important, was opened in 1888 by Nuttall, working in Flügge's laboratory, by his systematic study of the antibacterial properties of the body-fluids, particularly of the blood-serum. It is true that there were previous indications of the power of fresh blood to kill bacteria; indeed, if one wishes to trace this matter historically to its roots, he must go back to John Hunter, who was quite familiar with the antiputrefactive power of fresh blood, although, of course, he knew nothing of bacteria. Hunter showed that putrefying fluid could be added in small quantity to fresh blood without setting up putrefaction, and in elaborating his favorite doctrine of the "living principle of the blood" he interested himself greatly in certain phenomena which, if interpreted in the light of our present knowledge, are clear anticipations of some recent findings.

After Nuttall our knowledge of the bactericidal power of the blood-serum was extended by Buchner and others, but the next advance of fundamental importance in this direction was Pfeiffer's discovery in 1894 of the quick extracellular disintegration and solution of cholera spirilla in the peritoneal cavity of immunized guinea-pigs, or in that of normal guinea-pigs treated with immune serum, and of the presence in the immune serum of a specific substance concerned in the bacteriolytic process, although by itself without bactericidal power.

In the meantime Behring had made his great discovery of antitoxic immunity and of the protective and curative value of antitoxic serum, and Ehrlich had done much to elucidate the nature of this form of immunity. It soon became apparent, however, that immunity from the great majority of bacterial infections does not depend in the main upon the antitoxic principle. The attention of bacteriologists, therefore, was drawn more and more to the so-called "Pfeiffer phenomenon," which was found to be of great general significance, and starting from this and especially from the investigation of the analogous and much more readily studied solution of red corpuscles by foreign serum, there has followed in rapid succession up to the present time a series of new and most interesting discoveries and conceptions with which are connected many names, but most prominently those of Metchnikoff and Bordet, and Ehrlich and Morgenroth.

Through these various studies of immunity we have become acquainted with an important physiological capacity of the healthy organism, the extent and in most instances the existence of which was unsuspected until quite recent years. This capacity is the power to produce substances specifically antagonistic to all sorts of foreign cells and cellular products and derivatives. The substances capable of inducing this immunizing re-

action appear to be mainly of an assimilable, albuminous nature, or at least intimately associated with such material, although it has been proved that certain non-albuminous derivatives of proteids have the same power.*

The mode of antagonism of the specific bodies formed in response to the reception within the living organism of substances capable of inducing the necessary reaction varies with the nature of these latter substances, and consists in such diverse manifestations as neutralization of poisons and of ferments, injury or destruction of cells, associated with characteristic morphological changes, cessation of motility of cells or their appendages, agglutination of cells, precipitation, and coagulation. In accordance with these different effects the corresponding antagonistic bodies, or anti-bodies as they are called, are classified as antitoxins, anti-enzymes, cytotoxins, agglutinins, precipitins, and coagulins, and even against these bodies, with the exception of the antitoxins, antagonists have in turn been produced. All of these bodies are in varying, but usually high degree specific with reference both to the nature and to the source of the material upon which they exert their characteristic effects.

The cytotoxins or cytolysins include not only the bacteriolysins and hemolysins, but also a great number of other cellular toxins present in the sera of animals which have received injections of cells from a different species. To every cellular group of an animal species there appears to correspond a specific cytotoxin. To designate these various cytotoxins such self-explanatory names as leucotoxin, spermotoxin, nephrotoxin, neurotoxin, thyreotoxin, syncytiotoxin are used. Their specificity extends not only to the nature of the cells but also to the species of animal furnishing the cells used for their production.

One of the most important results of recent work is the separation of these specific anti-bodies into two groups, in one of which, represented by the antitoxins, the antagonists are single bodies; while in the other, represented by the cytolysins, the antagonistic effect requires the cooperation of two bodies. Of these two bodies the one which actually destroys the foreign cells or induces other specific effect is normally present in the cells or fluids of the organism, but it seems incapable of action without the intermediation of a body which is distinguished from it by greater resistance to heat, and which is produced by the immunizing reaction, although it may also be normally present in smaller amount.† The two elements composing a cytolysin exist quite independently of each other, so that one may be present without the other or be artificially removed without affecting the other. Of the multitude of names proposed for these cytolytic components, those most commonly used for the body which is the specific product of immunization, although it may also exist normally, are intermediary body, immune body, amboceptor, sensitizer, fixative, preparative, desmon, and for the other body complement, alexin, cytase. It is this latter body which contains the atomic group described as toxophoric or zymophoric.

Concerning the source, mode of action and constitution of the specific antagonistic bodies we are very imperfectly informed. That they are of cellular origin seems certain, and Ehrlich, with great ingenuity, on the basis of a brilliant series of experiments, has advanced an hypothesis regarding them which, in my opinion, better than any other hitherto suggested accords with the known facts and in promoting discovery has already done the greatest service of which a working hypothesis is capable. Ehrlich has so recently and so fully in the Croonian lecture presented before English readers his hypothesis of the side-chains or receptors and the basis for it, that I need only recall to your minds his conceptions that the toxins, cells and other substances which lead within the living body to the production of antitoxins, cytolysins and other antagonists have this capacity only through the possession of specific affinities, called haptophore groups, for corresponding haptophore groups belonging to side-chains or receptors of certain cellular constituents of the body, and that, in consequence of this appropriation of receptors, others of like nature are produced in excess of the needs of the cell, and these, being shed into the lymph and blood, there constitute the antitoxins, intermediary bodies, agglutinins and other specific antagonists. The antitoxic receptor has only a single combining affinity, which is for the toxin; whereas the cast-off receptors constituting the intermediary bodies of cytolysins have at least two affinities (hence called amboceptors by Ehrlich), one of a more highly specialized nature being for the invading bacteria or other foreign cells, and the other for the complement.* The anti-body enters quantitatively into definite chemical union with its affinitive substance.

The essence of Ehrlich's theory concerning antitoxin is thus tersely expressed by Behring: "The same substance which, when incorporated in

*Specific precipitins have been produced by injection of crystalline and other so-called pure proteids. Obermayer and Pick produced immune bodies by the use of non-albuminous products of tryptic digestion of certain albumins. Jacoby has shown that the specific body concerned in ricin immunization is non-albuminous. Klein obtained entirely negative results with injections of starch, glycogen, glucose, gum-arabic, and gelatine.

†Metchnikoff believes that the complement or cytase, which in his opinion exists under normal conditions solely within cells, not free in the plasma, acts in natural immunity without the cooperation of an intermediary body or fixative, the latter being concerned only in acquired or artificial immunity. The evidence seems, however, to favor the view that in this regard the conditions are similar in both forms of immunity, the main difference being the presence of a much larger amount of the specific immune body in the latter.

*According to Ehrlich's latest conception, resulting from investigations to demonstrate the multiplicity of complements, an amboceptor has a single cytophilic affinity and a number of complementophilic affinities differing in their avidity for various complements. He regards the agglutinins, precipitins and coagulins as uniceptors of more complex structure than the antitoxins, but Bail has recently brought evidence to show that agglutinins, like cytolysins, are composed of two elements. For the purposes of this lecture it is not deemed necessary to enter into these or many other details of this complicated subject. For comprehensive and admirable critical reviews of recent theories of immunity and Ehrlich's hypothesis of the receptors, I would refer to Professor Ritchie's papers in "The Journal of Hygiene," Vol. II., No. 2, and succeeding numbers, and to Dr. Aschoff's paper in Zeitschrift f. allgem. Physiologie, Bd. III., Heft 3.

the cells of the living body, is the prerequisite and condition for an intoxication becomes the means of cure when it exists in the circulating blood." So of the twofold bactericidal and cytolytic agents we may say that the living body possesses substances which may protect it by destruction of invaders, or may injure it by destruction of its own cells, according to the mates with which these substances are joined.

An inquiry which naturally arises in this connection is: What is the physiological mechanism called into action in the processes resulting in the production of antitoxins, cytolysins, and similar bodies? We have no reason to suppose that the animal body is endowed with properties specially designed to meet pathological emergencies. Its sole weapons of defense, often lamentably imperfect for morbid states, are adapted primarily to physiological uses.* To the foregoing inquiry Ehrlich answers that the mechanism concerned is one physiologically employed for the assimilation by the cells of food. The receptors are in the cells not for the purpose of linking poisons to the cells, but to seize certain food-stuffs, particularly the proteids, and the toxins and bacterial and other foreign cellular substances, if capable of inducing the immunizing reaction, chance to have the requisite combining affinities for the food-receptors. It is interesting that Metchnikoff also, though from a different point of view, refers the mechanism of immunity to the physiological function of assimilation of food by the cells.

Inasmuch as according to Ehrlich's hypothesis the specific antagonistic substances resulting from the injection of toxins and of foreign cells or derivatives of cells exist preformed in cells of the normal body, there would appear to be no reason why any one of them might not occasionally be present normally free in the blood or fluids. In fact, many of them, such as diphtheria and tetanus antitoxins, various anti-enzymes, bactericidal, hemolytic and other cellular toxins, agglutinins, and a number of other bodies of this class as well as their anti-bodies, have been found repeatedly, though, of course, in the case of many inconstantly and with marked differences between individuals and species, in the blood of healthy human beings or animals when their presence could not reasonably be attributed to a previous specific immunization. Of these normal anti-bodies the only one which is increased in amount by the process of immunization is that specifically related to the material used to bring about the reaction. As already stated, it is the intermediary body,† not the complement, which is generated in immunization against bacteria and other cells.

The foregoing statements, though of necessity condensed and incomplete, about the general characters of the specific anti-bodies will, I trust, help to a better understanding of what is to follow concerning the bearing of some of these discoveries on medical science and practice. I realize the difficulties which you must already ploring the multiplication of unnecessary new lines of research, in following a brief presentation of a subject in which not only are the facts so complex and the ideas so novel, but the terminology so strange and burdened with such a multitude of confusing synonyms. While dehave experienced, if unfamiliar with these new terms, I should like to quote in this connection a wise remark of Huxley*: "If we find that the ascertainment of the order of nature is facilitated by using one terminology, or one set of symbols, rather than another, it is our clear duty to use the former; and no harm can accrue so long as we bear in mind that we are dealing merely with terms and symbols."

The most remarkable and characteristic attribute of these anti-bodies is the specificity of their relation to the substances which have led to their formation. Of some of them, such as diphtheria or tetanus antitoxin, this specificity is nearly absolute; of others, such as the precipitins, it is only relative. This property is the basis of new and most valuable methods for the identification of species and the determination of genetic relations—species not only of living things, but also of chemical substances and of disease.

The resemblances and the differences thus revealed are doubtless fundamentally of a physicochemical nature, but in many instances they transcend the powers of the microscope or of ordinary chemical tests to detect.

The results already attained by the method of serum diagnosis,† using this expression in its widest sense, are not only of interest and importance to the biologist, physiologist, and chemist, but of great practical value to the bacteriologist and the physician. As this is not an aspect of my subject, broad and important as it is, upon the details of which I propose to dwell, it must suffice to present by way of illustration examples of the diagnostic application of different kinds of specific sera.

The only means of detecting toxins of the class of diphtheria or tetanus toxin, snake-venom, and certain vegetable poisons of the same category is their neutralization by the corresponding antitoxic sera. Occasion may arise where such detection is of practical and even medicolegal importance, as has been exemplified in India, where the criminal use of cobra-venom is not unknown.

*W. H. Welch. Adaptation in Pathological Processes. Trans. Congress American Physicians and Surgeons, 1897. Vol. IV.

†I use in this lecture the name "intermediary body" in preference to the more technical term "amboceptor," although Ehrlich applies the German equivalent—Zwischenkörper—only to normal as distinguished from immune amboceptors.

*Huxley. On the Physical Basis of Life. Collected Essays. Vol. I., p. 164. New York, 1893.

†The general procedure followed in the production of specific sera is the injection into a suitable animal at intervals of time repeated doses of toxins, bacteria, foreign cells or other material against which the anti-body is desired. For example if a specific precipitating or a hemolytic serum for human blood is wanted, an animal, say a rabbit, is injected subcutaneously or intraperitoneally at intervals of three or more days with five or six doses of human serum or human red blood-corpuscles. At the end of this time the rabbit's serum has acquired the property of precipitating in strong dilutions human serum, or of dissolving human red blood-corpuscles, if these were used for the injection. Within limits the less closely related the two species of animals, the more powerful is the antagonistic effect of the specific serum. This is true especially in the case of cytotoxic sera.

The application of serum diagnosis which is most familiar to physicians is the agglutinative test for typhoid fever. The principles of the agglutinative reaction were worked out in the laboratory of Professor Gruber in Vienna by himself and Durham, and were there first applied to the diagnosis of typhoid fever by Greenbaum, who was anticipated in his publication by Widal, who has made a thorough clinical study of the subject. The method is of great value, not only in the diagnosis of disease, but also in the identification of bacterial species and the recognition of relationships between species. Durham, to whom we owe important contributions to this subject, has given an ingenious hypothetical explanation of mutual agglutinative reactions, the main features of which are paralleled in Ehrlich and Morgenroth's doctrine, based upon experiments, relating to the multiplicity of cell-receptors and of amboceptors concerned in hemolysis.*

We have found the agglutinative reaction an indispensable aid in the study of the series of cases of paratyphoid fever which have come under observation in Dr. Osler's wards at the Johns Hopkins Hospital, and which otherwise it would have been scarcely possible to have separated from typhoid fever.† The occurrence of paratyphoid fever as a distinct disease affords an explanation of a certain proportion of the failures of the serum from supposed typhoid patients to clump typhoid bacilli. Not less valuable is the serum test in the diagnosis of *Bacillus dysenteriæ Shiga* and of the diseases caused by it. This microorganism has been shown by Flexner and his pupils, Vedder and Duval, to be the cause of our acute dysenteries, and recently in Baltimore Duval and Bassett, working with the aid of the Rockefeller Institute for Medical Research at the Thomas Wilson Sanitarium for Children, have discovered that this same bacillus is in all probability the specific agent of infection in the summer diarrheas of infants.

Bacteriolytic sera have been used by Pfeiffer in the differentiation of cholera and allied spirilla, but few other bacteria present equally well the Pfeiffer reaction, which is not nearly so useful or handy a means of identification as the Gruber-Durham reaction.

Of other cytolytic sera the hemolysins have been by far the most carefully studied. One of the most interesting results of this study has been the determination by precise quantitative methods of resemblances and of differences between red blood-corpuscles which in no other way could be distinguished. These resemblances and differences relate to the red corpuscles not only of different species of animals, but also to those of individuals of the same species. Although we constantly assume the existence of cellular differences between individuals and between species, these are for the most part of so subtile a nature as to elude our methods of observation. The exact demonstration of such differences by the use of cytolytic sera is therefore of especial interest. My assistant, Dr. Marshall, in an unpublished research, conducted under the direction of Professor Ehrlich and Dr. Morgenroth, upon the receptors of the red blood-corpuscles of man and of two species of monkey, found that while man and the monkeys each have receptors not shared by the other they also have a large number of receptors in common.

This result is in harmony with Nuttall's interesting observations on a much more extended scale regarding phylogenetic relationships between animal species as shown by the reaction of their blood with the specific precipitins discovered by Tchistowitch and Bordet and introduced into practical medicine by Wassermann. This biological test to determine the source of blood, when used with proper precautions, far surpasses in accuracy all other methods for this end. While it would lead too far from my purpose to follow this subject farther, I cannot in this connection forbear at least mentioning one of the earliest and most suggestive papers on this class of anti-bodies, that "On Immunity against Proteids" by Walter Myers, who gave up his life in the cause of science and of humanity, and whose early death is so great a loss to English medical science.

I shall ask your attentions now to some considerations concerning the bearing of recent studies of immunity on the nature and action of toxins. This subject is of course of the greatest pathological as well as bacteriological importance, and I believe a closer cooperation than now exists between bacteriologists and pathologists in its study would further the surer and more rapid advancement for our knowledge about it. One misses only too often in purely bacteriological papers on this subject exact knowledge and descriptions of pathological conditions, and on the other hand pathologists often fail to utilize pertinent facts and ideas which are familiar to bacteriologists.

The discovery by Roux and Yersin of the diphtheria toxin, the studies by Behring and Kitasato of tetanus toxin leading up to Behring's epochal discovery of antitoxin, and the later investigations of Ehrlich on the constitution of diphtheria toxin and the origin and mode of action of antitoxin are the great events in the most brilliant and securely founded chapter of modern studies of immunity. Through these researches we became acquainted with a class of poisons secreted by certain bacteria and present in solution in culture fluids. The evidence is conclusive that these soluble toxins enter, as assimilable substances, into direct combination with constituents of the body-cells for which they have an affinity, and only thereby are enabled to bring about immunity or to exert toxic effects. As shown by the modifications of toxins called

*Durham. Journal of Experimental Medicine, Jan. 15, 1901. Vol. V., p. 353. Ehrlich and Morgenroth. Berliner klin. Wochenschr., May 27, 1901, p. 570.

†See papers on paratyphoid fever by Johnston, Hewlett and Longcope in American Journal of Medical Sciences, August, 1902.

toxoids, the toxic property may be lost without loss of the combining power and without removal of the immunizing power. According to Ehrlich's helpful conception, based on a large amount of experimental evidence and now very generally accepted, the combining power of the toxin molecule resides in a group of atoms, designated as the haptophore group, with affinity for the corresponding haptophore groups of the side-chains or receptors of cellular constituents, and the toxic power pertains to another and less stable atom-complex in the molecule.

By means of these facts and legitimate deductions from them we are enabled to explain in a satisfactory way susceptibility to poisoning by these soluble toxins, their selective action upon the cells of the body, and their quick disappearance after injection into the circulating blood. In one infectious disease and in one only, to wit, tetanus, are we able to explain the clinical and pathological phenomena in minute detail on the basis of our knowledge of the causative microorganism and its poisonous products. The nearest approach to this instance is diphtheria, but here we have not yet been able to follow the trail of the toxins within the body so perfectly, and, as Flexner and I have shown, in addition to the soluble toxins there is an intracellular poison concerned in the production of the false membrane. Interesting investigations, which have greatly helped to elucidate the nature of these toxins, have been made on various similar vegetable and animal poisons, such as ricin and abrin from the former source, and the venom of snakes, spiders and other poisonous animals.

The high hopes which were raised by the discovery of the soluble bacterial toxins that at last the way was opened for us to penetrate into the mysteries of the mode of action of pathogenic bacteria were soon doomed to disappointment, for similar powerful toxins, though diligently sought, could not be detected in the cultures of most other bacteria, and these among the most important ones, such as the tubercle bacillus, the typhoid bacillus, the cholera spirillum, the pneumococcus, the pyogenic micrococci. This disappointment was all the more acute because there was and is every ground for confidence that whenever we have in our possession a powerful toxin of this class a strong protective antitoxic serum can readily be obtained.

Notwithstanding these negative results the belief was not abandoned that bacteria harm the body mainly by poisoning, for it rests upon strong clinical and pathological evidence, as well as upon the study of the distribution of bacteria in the infected body. The search for poisons was turned from the fluid part of cultures to the bacteria themselves, and thus Pfeiffer succeeded in demonstrating as an integral constituent of the bodies of cholera spirilla, toxic substances which are liberated only when the bacteria degenerate or die. Intracellular poisons, which indeed previously, though of a different nature, had been extracted from bacteria by Buchner and by Koch, were subsequently found within typhoid bacilli and a number of other pathogenic bacteria.

It is of more than purely bacteriological interest to recognize the distinction between the small group of pathogenic bacteria, represented by the bacilli of tetanus, of diphtheria, and of botulism, characterized by the secretion of powerful soluble toxins, and the much larger group, containing most of the other pathogenic bacteria, which do not secrete similar strong toxins, for it is only the former which give rise to the production of antitoxic sera of marked protective and curative power.

The form of immunity resulting from injections or natural infections with the second class of bacteria belongs mainly to the bacteriolytic type, in which, you will recall, the complete antibody is not a single substance, like antitoxin, but is composed of two distinct elements, intermediary body and complement, of which only the former is produced or increased in the process of immunization. The bacteriolytic sera are also under suitable but not readily controlled conditions protective and curative; but owing, it would seem, mainly to the duplex nature of the antibody their successful therapeutic application meets difficulties which have not yet been overcome. The great practical problem of bacteriology to-day is to make available to medical practice the bacteriolytic sera, such as antityphoid, antipneumococccus, antistreptococcus, antiplague, antidysentery sera. Such work as that of Marmorek, of Wassermann, of Neisser and Wechsberg, or Ainley Walker upon the production, the properties, the conditions underlying the action of these sera is, therefore, highly important.

Our knowledge of the constitution and action of the intracellular bacterial poisons is most incomplete, and at present cannot be applied in any very definite and satisfactory way to the explanation of the morbid phenomena of infectious diseases. Such investigations as those undertaken by Macfayden and Rowland at the Jenner Institute of Preventive Medicine upon the expressed juices of bacterial cells promise to shed light upon this subject and in general upon the vital processes of bacteria.

I find it difficult to reconcile myself to the doctrine that bacteria such as the typhoid bacillus, the pneumococcus, and others of the class now under consideration do their chief injury to the body, not while they are lively and vigorous, but after they become corpses, and in consequence set free their protoplasmic poisons. Still this latter conception is the basis of a coherent hypothesis of infection, elaborated most fully recently by Radziewsky,* which rests upon a considerable amount of accurate observation and interesting experimental work. There can be no doubt that in the course of many infections there goes on an enormous destruction of the bacteria concerned, so that the numbers of those indicated at any given time by microscopical ex-

*Radziewsky. Zeitschr. f. Hygiene, 1900, XXXIV, p. 185, and 1901, XXXVII, p. 1.

amination and by cultures may represent only an insignificant fraction of the total progeny of the first invaders. I have been much interested in this phenomenon since I became familiar with it over twelve years ago.† in pneumococcus infections through the employment of a method which revealed in the exudates degenerating and dead pneumococci and their empty capsules in numbers often far exceeding the intact organisms, indeed in some cases so many that they formed a large part of the exudate.

While all due weight should be given to such facts as these, the objections to the acceptance of the hypothesis just mentioned as affording a complete explanation of the toxic phenomena of this class of infections are so obvious that naturally efforts have been made to learn whether bacteria which produce no strong soluble toxins in our ordinary culture media may not do so on other media of special composition, or in a demonstrable way within the living body. Work in these two directions has not been altogether barren, as shown by results of experiments made by Hueppe, Cartwright Wood, Marmorek, and others, along the former lines, and by Metchnikoff, Roux and Salimbeni along the latter, but it cannot be said that these experiments have led to any generally accepted solution of the main difficulties. Some are therefore inclined to lay the chief emphasis upon disordered cellular metabolism, but this is only a restatement of the question. Everybody recognizes abnormal metabolism as an essential condition in infections. The very point needing explanation is how the bacteria derange metabolism.

I wish here to advance an hypothesis which seems competent to explain the source, the mode of production, and the nature of certain bacterial toxins. It would appear to be a natural inference from the receptor theory of Ehrlich and the recent work on cytotoxins. The following considerations will, I hope, make clear the essential points.

As I have already stated, we know that the injection of foreign cells, such as pathogenic bacteria, red blood-corpuscles, spermatozoa, epithelium, into the tissues of an animal leads to the formation of poisons, called cytotoxins, acting specifically upon these cells; that the substances which stimulate the cells of the host to produce one constituent of this class of toxins consists of certain atom-complexes derived from the injected cells; that certain cells of the host thus stimulated generate and discharge one component of the toxin, called the intermediary body, which becomes the medium of intoxication through union, on the one hand, with a preexistent toxophore substance, called the complement, and, on the other hand, with the foreign cell which started the reaction.

Such is the response on the part of the host to the entrance of the foreign cells, but how about a possible response of a like nature on the part of the invading cells toward the host, resulting in the production of special cytotoxins, of analogous constitution, injurious to the host? This latter response, being of a vital nature, can take place only when the invading cells are living, as in the case of bacteria and other parasites. I see no reason why suitable substances derived from the host may not stimulate parasitic organisms, through a physiological mechanism similar to that operative in the development of cytolytic immunity, to the production of intermediary bodies, which, if provided with the requisite affinities, have the power to link complements to cellular constituents of the host and thereby to poison the latter. Expressed in terms of Ehrlich's side-chain theory, certain substances of the host of cellular origin, assimilable by the parasites through the possession of haptophore groups with the proper affinities, become anchored to receptors of the parasitic cell, which, if not too much damaged, is thereby stimulated to the overproduction of like receptors; these excessive receptors of the parasite, if cast off into the fluids or the cells of the host, there constitute intermediary bodies or amboceptors with special affinities for those cellular constituents or derivatives of the host which led to their production, and for others which possess in whole or in part identical receptors. Provided the host is supplied also with the appropriate complements there result cytotoxins with special affinities for certain definite cells or substances of cellular origin in the host. The contribution of the parasitic cells to these cytotoxins is the amboceptors. Either the parasite or the host may provide the complements.*

It may perhaps aid in grasping the ideas here presented to imagine the bacterium, in the capacity of the host, as a structure so large that one could inject into it animal cells. Provided the proper receptor apparatus is present, the resulting reaction on the part of the bacterium, as described, would be a process of immunization against the animal cells through the formation of specific cellulicidal substances. In reality it is only certain atomic complexes of cells which are concerned in this immunizing reaction, and in comparison with these even the smallest bacterium is a gigantic object.

Looked at from the point of view of the bacterium, as well as from that of the animal host, according to the hypothesis advanced, the struggle between the bacteria and the body-cells in infections may be conceived as an immunizing contest in which each participant is stimulated by its opponent to the producton of cytotoxins hostile to the other, and thereby endeavors to make itself immune against its antagonist. These mutually antagonistic cytotoxins are capable of injuring the parasitic cells, on the one hand, or the body-cells, on the other, only when, escaping

†Welch. Bulletin of the Johns Hopkins Hospital, July, 1890, and December, 1892.
Michaelis (Berliner klin. Wochenschr., 1902, No. 20) has recently reported similar findings.

*We may thus speak of xenogenic cytotoxins resulting from the action of bacterial stimuli on cells of the host, and of bacteriogenic cytotoxins from xenogenic stimuli, also of xenogenic and bacteriogenic complements.

combination outside of them, they are anchored to the receptors of the cells to which their respective affinities are adjusted. This combination with the cells, if it does not result in too great injury to them, is the condition for further production of the cytotoxic intermediary bodies through overproduction and discharge of receptors.* The important factors determining the issue of the contest are the relative proportions and the distribution of the bacterial and the host's cytotoxins.

The hypothesis thus outlined can be tested experimentally, but I regret that it has shaped itself in my mind so recently that I have not yet been able to make the desired experiments, which are, however, now started in my laboratory. Since my arrival here I am informed that these experiments have already furnished facts in its support.

Inasmuch as at least one component, and it may be both components, of the assumed bacterial cytotoxins preexist in the bacterial cells, it should be possible to demonstrate some of them in artificial cultures of bacteria, where they would be found especially as integral parts of the cells, unless extracted from the bodies of degenerating or dead bacteria. This corresponds with what is known concerning the situation of the poisons of the cholera spirillum, the typhoid bacillus, and other bacteria characterized by the lack of strong soluble toxins. But the quantitative and other relations between these cultural cytotoxins and those produced, in the manner described, by the same bacteria during processes of infection are comparable to those between the normal anti-bodies and the immune anti-bodies. These relations would explain the familiar fact that cultures of bacteria of the class under consideration constitute in genral only a partial and meager index of the toxic capacities of the same bacteria in the infected body. That cytolysins may, however, be present normally in large amount is illustrated by the hemolysins of eel's serum and of snake-venom.

In this theory degenerated and dead bacteria, while recognized as a source of poisoning in infections, are not assigned an exclusive rôle in this regard. Living bacteria in the infected body, where they are under nutritive conditions not paralleled in artificial cultures, actively produce and secrete receptors which may become the means of intoxication of the body-cells. From what has been said, we can comprehend how these diverse free receptors may enter into the formation of cytotoxins of the most varied and specific characters, such as erythotoxins, leucotoxins, neurotoxins, nephrotoxins, spermotoxins, hepatotoxins, etc. Very probably in many instances these toxins are represented by so few receptors in bacterial cells in ordinary cultures that it would be hopeless to search for them there, although we may have convincing experimental and pathological evidence that within the animal body the same bacteria produce them abundantly under the stimulus of appropriate substances derived from cells of the host.

The methods hitherto employed for the study of bacterial poisons have not generally been calculated to reveal the presence of toxins with the characters indicated, even if such existed in the cultures. Recently, however, a beginning has been made in this direction, and we have already become acquainted with certain toxins of an interesting nature, to which I desire to direct your attention.

Intrinsically, and in their general bearing upon the subject before us, the recent investigations of Flexner and Noguchi upon the constitution of the toxins in snake-venom are of especial importance. It was in snake-venom that Weir Mitchell and Reichert first demonstrated the existence of that class of poisons often called, although with doubtful propriety, toxic albumins. Investigations of snake toxins are of peculiar interest for many reasons not the least of which is their resemblance to bacterial toxins. The demonstration by Sewall of the possibility of active immunization from venom and the further studies by Calmette and Fraser of this phenomenon, and especially of the protective and curative properties of antivenin, are well known.

Until recently it has been generally held that the venom toxins resemble in molecular structure the diphtheria and the tetanus toxins in being single bodies with a combining or haptophore group and a toxophore group of atoms. The researches of Flexner and Noguchi, now in progress, of which only the first part has been published,* necessitate a quite different conception of the nature and manner of action of venom toxins than that previously entertained. I have

*It will be observed that these discharged receptors may be regarded as the equivalents of anti-immune bodies. E. W. Ainley Walker in an interesting and suggestive paper on "Immunization against Immune Sera" (Journal of Pathology and Bacteriology, March, 1902) shows experimentally that bacteria growing in immune sera produce anti-immune bodies and thereby become more virulent. He concludes that "the basis of bacterial virulence and of chemiotactic influence is identical, and constitutes that atom-group which causes the production of the immune body." My hypothesis includes the conception supported by Walker and also much more. According to the hypothesis certain anti-bodies of bacterial origin are capable not only of neutralizing immune bodies of the host but with the aid of complements also of poisoning the cells of the host. It is not difficult to imagine various conditions in which the anti-bodies of bacterial origin may escape neutralization before entering into union with the host's cells. The substances which stimulate bacteria to produce these anti-bodies need not necessarily be toxic to them; in fact, toxicity, such as that of strong bactericides of cellular origin, would hinder their production. The essential things are that the stimulating substances have the requisite combining groups for bacterial receptors, and that the cast-off receptors be complemented within the body of the host.

Each of the various bacteriogenic cytotoxins probably contains a multitude of partial amboceptors with varying cytophilic and complementophilic affinities, in accordance with the views of Ehrlich and Morgenroth.

It is self-evident that through a mechanism similar to that described parasites within the infected body may be stimulated by atom-groups derived from the host to the production also of anti-bodies other than cytotoxins, such as various agglutinins, precipitins, anti-enzymes, and perhaps of uniceptors of the nature of secreted, soluble toxins, or of enzymes, all adjusted against the host.

Questions relating to the source and nature of the complements, particularly of intracellular complements, and also to anticomplements, are manifestly of importance in relation to the hypothesis, but it would complicate the subject too much to discuss these and other matters here, where my purpose is merely to outline the essential features of this new theory of infection with reference to the particular points under consideration.

*Flexner and Noguchi. Snake Venom in Relation to Hemolysis, Bacteriolysis, and Toxicity. Journal of Experimental Medicine, March 17, 1902. Vol. VI., p. 277.

followed with great interest the work of Professor Flexner on toxins, begun several years ago in my laboratory when he was my assistant and associate, and since continued along new lines in his laboratory at the University of Pennsylvania, and I wish to acknowledge his generosity in permitting me to use in this lecture certain unpublished results of his and Noguchi's investigations.

These investigations have shown that the toxic action of venom upon red blood-corpuscles, leucocytes, nerve-cells, and other cells is like that of the duplex cytotoxins already described; that is, it depends upon the combination of intermediary bodies contained in the venom, on the one hand with the animal cells for which these bodies respectively have affinities, and on the other hand with corresponding complements contained, not in the venom, but in the cells or fluids of the animal acted on. For example, it is well known that the addition of venoms to fresh blood brings about the quick destruction and solution of the red corpuscles. If, however, certain venoms be added to red corpuscles which have been thoroughly washed with isotonic salt solution, so as to remove all the complement, the corpuscles are agglutinated but not dissolved, although it can be shown that substances from the venom (intermediary bodies) have entered into combination with the corpuscles. If now a little fresh serum, which contains the complement and by itself may be an excellent preservative of normal corpuscles, be added to these venomized corpuscles, they are promptly dissolved.

Preston Kyes, working in Professor Ehrlich's laboratory, in an investigation just published* on the mode of action of cobra-venom, confirms the conclusion of Flexner and Noguchi concerning the amboceptor nature of cobra-venom, and adds much that is new and important to our knowledge of this subject. He finds that the washed blood-corpuscles of certain animals are directly dissolved by cobra-venom, while those of other animal species require the subsequent addition of complements or adjuvants to bring them under the influence of the venom. But even in the former case a complementary body is essential to the reaction, this, however, being not a serum complement, but an endocomplement contained within the red blood-corpuscles. Of great significance is the demonstration by Kyes of still a third substance, namely, lecithin, which is capable through combination with the venom intermediary body of completing the hemolytic potency of venom.† The discovery for the first time of a definite, crystallizable substance with the power of uniting, like a complement, with an intermediary body, and thus completing the formation of a cytotoxin, is evidently of fundamental importance. The suggestion by Ehrlich and Kyes that possibly the cholin group is the toxophore group of lecithin is particularly interesting in the light of F. W. Mott's valuable studies of chemical processes concerned in degenerations of the nervous system.

The researches of Flexner and Noguchi and of Kyes therefore have taught us that in poisoning by venom the bodies of human beings and of animals contain in the form of complements, or alexins* as they are also called, the substances which are most directly concerned in the act of poisoning. The venom serves merely to bring into the necessary relations with constituents of the body-cells poisons we already harbor or may generate, but which are harmless without the intervention of intermediary bodies. These poisons within us are powerful weapons which, when seized by hostile hands, may be turned with deadly effect against our own cells, but which are also our main defense against parasitic invaders. We see here as everywhere that nature is neither kind nor cruel but simply obedient to law.

Flexner and Noguchi have demonstrated experimentally that, like the hemolytic, so also the leucotoxic, the neurotoxic, and other cycotoxic properties of venom depend upon combinations of venom intermediary bodies with complements contained in the cells poisoned by venom or in the fluids bathing these cells. Particularly striking are their experiments showing in vitro and under the microscope the cytolytic action of cobra-venom upon certain large molluscan nerve-cells in the fresh state. The complement essential to this reaction is contained within the nerve-cells. In previous experiments of Flexner and Noguchi there had been indications that a special class of intracellular complements are concerned in some of the toxic effects of venom upon cells. The positive demonstration by Preston Kyes of a special class of intracellular complements or endocomplements is unquestionably of great pathological interest, and seems destined to play an important part in the explanation of many morbid conditions both in connection with endogenic and exogenic intoxications, probably also in such phenomena as self-digestion or autolysis.

Snake-venom is a rich mine of diverse toxins, and, on account of its pathological importance, I must mention one of the cytotoxins discovered there by Flexner and Noguchi, as it may be that a similar toxin is produced by certain bacteria and under still other conditions. As is well known, one of the most striking lesions resulting from poisoning by certain venoms is the occurrence of abundant hemorrhages in various tissues of the body. This effect has been generally attributed to the direct action of venom on the red corpuscles and on the coagulability of the blood, but the experiments of Flexner and Nogu-

*Preston Kyes. Ueber die Wirkungsweise des Cobragiftes (Berliner klin. Wochenschr., 1902, Nos. 38 and 39). I am greatly indebted to my friend Professor Ehrlich and to my former pupil Dr. Kyes in putting me in possession of the main results of these interesting experiments before the date of their publication.

†The objections made by Calmette (Compt. rend. Acad. d. Sc., 1902, T. 134, No. 24) to Flexner and Noguchi's interpretation of their experiments as to the amboceptor nature of venom have been completely overthrown by the experiments of Preston Kyes.

*There is some objection to the use of the term "alexin" as a synonym for "complement," as the former was applied originally by Buchner to substances which we now know to be combinations of complements with intermediary bodies.

chi indicate that these hemorrhages are due to the presence in venom of a cytotoxin which has the power of dissolving endothelial cells, in other words an endotheliolysin. Dr. Flexner suggests the name "hemorrhagin" for this special toxin, which causes extravasations of blood through its direct solvent action upon capillary endothelium, an effect which is readily demonstrable under the microscope. It is hardly necessary for me to stop to emphasize the clinical and pathological importance of the discovery of an endotheliotoxin, a kind of poison which may prove to be of special significance in the interesting group of hemorrhagic infections, and perhaps also in purpura and kindred affections.

The foregoing newly discovered facts, which I have sketched only in bare outline, illustrate in a striking way the fruitfulness of methods and conceptions which we owe to recent studies of immunity. The results of these investigations, however, are significant beyond the mere facts disclosed, important as these are. They have for the first time revealed in normal toxic secretions, readily introduced under conditions of nature into the tissues of man and animals, cellular poisons akin to the complex hemolysins, neurotoxins and other cytotoxins of immune and some normal sera, which have aroused so much interest and experimental study during the past four years. The most noticeable difference between the venom cytotoxins and those hitherto observed in immune sera is the far greater resistance to heat of the intermediary bodies of the former, but we are already acquainted with considerable variations in the sensitiveness to heat both of different intermediary bodies and of complements. That snake-venom should contain only one half of the complete poison, the other and the really destructive half being widely distributed in the blood and cells of man and of animals, is an instance of a curious kind of adaptation, of interest from evolutionary, as well as from other points of view.

In consideration of the often emphasized analogies between venom toxins and bacterial toxins, these facts render it highly desirable to make a systematic search of bacterial cultures by proper methods and under suitable conditions for complex cytotoxins. At present substances of this nature are not known to exist in our cultures. There have been discovered, however, within the past three or four years certain bacterial toxins which have a curious resemblance in some of their properties to the complex antibodies of blood, although, so far as they have been carefully studied, they appear to have the simpler constitution of the soluble toxins, like those of diphtheria and of tetanus. I refer to the bacterial hemolysins, leucolysins, hemagglutinins, precipitins and coagulins. There is no reason to suppose that this list exhausts the number of those actually present, for it is evident that it includes chiefly bodies readily demonstrable in test-tube experiments. It would be surprising if cytotoxins which act specifically upon red and white blood-corpuscles were the only ones of this class produced by bacteria; in fact, we have every reason from pathological observations to believe the contrary.

It has become evident that more refined methods than mere observation of the coarse effects of injecting into animals the filtrates or the killed bacteria of our cultures are required for the detection of the subtler and more specific cellular poisons. Instances are rapidly increasing in which by improved methods, cultures of bacterial species once believed to be practically devoid of toxicity are found after all not to be so poor in toxins, even of the soluble variety. One of the earliest and most instructive illustrations of this is the discovery by Van der Velde of a leucocyte-destroying poison, named leucocidin, in exudates caused by infection with *Staphylococcus aureus*, and also in filtrates of staphylococcus cultures, which had been previously regarded as almost if not entirely free from toxic power.

More widely distributed in cultures of different species of bacteria are the hemolysins of which the first example, discovered in 1898 by Ehrlich in cultures of the tetanus bacillus, was carefully studied by Madsen the following year, and which have since been investigated by Kraus with Clairmont and with Ludwig, Bulloch and Hunter, Neisser and Wechsberg, Todd, Besredka, and others. The list of bacterial species known to produce in cultures substances of this nature capable of dissolving red blood-corpuscles is already a long one and includes the bacilli of tetanus, of green pus, of typhoid fever, of acute dysentery, of diphtheria, of plague, the pyogenic staphylococci and streptococci, the pneumococcus and many other bacteria. Nuttall and I noted in our first description of *Bacillus aërogenes capsulatus* over ten years ago its capacity of laking blood so that I was not surprised to find recently that a hemolysin can be demonstrated in cultures of this organism. The blood-destroying property appears to stand in no definite relation to virulence, nor is it limited to pathogenic bacteria. It pertains also to many putrefactive bacteria. The strongest bacterial hemolysin hitherto observed was found by Todd in cultures of *Bacillus megatherium*, which is a widely distributed saprophyte.

As already stated, none of these bodies has been shown to belong to the class of complex hemolysins in blood, which have been far more exhaustively investigated than any other of the specific anti-bodies. Doubtless there is at present among bacteriologists too great a tendency to attribute to the less carefully studied anti-bodies characters which have been worked out in detail only for the hemolysins of immune serum. It would lead too far to attempt here a discussion of the special characters of the various bacterial hemolysins, which present in different specimens curious and at present unexplained divergencies as regards resistance to heat and several other properties. It must suffice to indicate briefly what

is known of the pathological importance of this interesting group of bacterial toxins.

In view of the abundant clinical and pathological evidence of extensive destruction of red corpuscles in the course of many infectious diseases, it is certainly significant to find that many bacteria are endowed with a specific hemolytic power. The question is how far we are justified in applying to the actual conditions of infection the existing experimental data upon this subject. Assuredly here, as everywhere, results of test-tube experiments, helpful in suggestion as they may be, should not be utilized without further evidence to explain morbid phenomena within the infected human or animal body. While much more work upon this subject is needed before our information will be exact or complete, the observations and experiments of Besredka,* Kraus and Ludwig† and others have already demonstrated that bacteria may exert their blood-destroying power within the living body. This hemolytic capacity of micro-organisms affords an explanation, although certainly not the only one, of the secondary anemias which are such a marked feature of many infectious diseases, as streptococcus and other septic anemies, pneumonia, typhoid fever, scarlatina and others. The hemoglobinuria which is a recognized, although rare complication of various infectious diseases may be referable to intoxication with unusually powerful bacterial hemoglysins, or to an exceptional lack of resistance of red corpuscles. Hemoglobin, however, is not necessarily present in solution in the blood-plasma, for the destruction of the damaged red corpuscles may take place within the large phagocytes of the spleen and the hemolymph glands, as is well known to occur on an extensive scale in typhoid fever and some other infections. A familiar example of the action of bacterial hemolysins is the postmortem reddening of the inner lining of the heart and blood-vessels, an effect which may be due to putrefactive bacteria, or may appear very soon after death, especially from septicemia caused by Streptococcus pyogenes which, as has been shown, may lake the blood during life.

The fact that certain common saprophytic bacteria may produce energetic hemolysins, as pointed out by Kraus and Clairmont and by Todd, has a possible bearing upon the etiology of certain obscure anemias not of infectious origin, particularly upon the interesting observations and the theory of William Hunter concerning their causation by absorption of toxins from the alimentary tract. Todd found cultures of *Bacillus megatherium* so strongly hemolytic that the intravenous injection of 1 c.c. of the filtrate into guinea-pigs was followed by hemoglobinuria, 10 c.c. being fatal. Human red corpuscles are sensitive to this hemolysin.

Normal human and other blood-sera contain in varying amounts antihemolysins, which protect the red corpuscles from the action of some of the bacterial hemolytic agents. Specific antihemolysins are readily produced by immunizing injections of bacterial hemolysins, and are generated also in the course of infections. Lang suggests that the augmentation of the osmotic resistance of the erythrocytes which has been noted in some infectious diseases, as well as in icterus and some other morbid conditions, may be a reactive phenomenon caused by the presence of hemolytic toxins.

Intimately associated with the hemolysins in cultures are the bacterial hemagglutinins (Kraus* and Ludwig*), substances which have the power to clump red blood-corpuscles. Among unicellular organisms both the capacity to produce agglutinins and the aptitude for agglutination seem to be very widely distributed. The bacterial hemagglutinins, in analogy with the bacterial hemolysins, are apparently of simpler constitution than the serum agglutinins, being destroyed at 58° C., whereas the latter are not injured by temperatures under 70° C. In order to demonstrate in cultures the hemagglutinins, it is generally necessary to eliminate in some way the action of the associated hemolysins, which can be done by using small quantities of the culture fluid or by keeping the mixture of fluid and red corpuscles at zero temperature.

I know of no observations directly demonstrative of the action of bacterial hemagglutinins within the living body in infections, but this subject is of such recent knowledge that it has been as yet scarcely investigated. Certainly there are morbid conditions which seem highly indicative of the operation of substances agglutinative of red corpuscles. Probably everyone with large experience in the examination of fresh blood in disease has noticed that sometimes red corpuscles, examined immediately after withdrawal of the blood, have a peculiar tendency to form clumps which cannot readily be broken up. This phenomenon, which is certainly suggestive of the action of an agglutinating agent, I have observed especially in some cases of septic infections and of cirrhosis of the liver.

Furthermore, I would emphasize the support given by the recognieion of hemagglutinins to views advocated many years ago by Hueter and by Klebs concerning the occurrence of thrombi composed of coalesced red blood-corpuscles. Such thrombi I believe to be not uncommon in typhoid fever and other infections, especially in small blood-vessels. I have elsewhere called attention to the evidence in favor of the interpretation of many of the hyaline thrombi as derived from agglutinated red corpuscles.

It can scarcely be doubted that substances agglutinative of white blood-corpuscles are also produced by certain bacteria and that these are concerned in the clumping of pus-cells and of leucocytes within the living body, but it would not be profitable to discuss this matter without more exact information than we now possess.

In this connection I may say that not only

*Besredka, Annales de l'Institut Pasteur, 1901, XV., p. 820.
†Kraus and Ludwig. Wiener klin. Wochenschr., 1902, p. 382.

*Kraus and Ludwig. Wiener klin. Wochenschr., 1902, p. 120.

the discovery of the bacterial hemagglutinins, but also that of the hemolysins and the leucolysins, is likely to shed new light upon certain aspects of the difficult subject of thrombosis. The red corpuscles undergo various morphological changes under the influence of different bacterial hemolysins acting with varying intensity. Distortions of shape, throwing out of projections, and detachment of colorless particles resembling platelets can sometimes be seen. These observations are of especial interest with reference to the doctrine, already strongly supported, that platelet thrombi originate from disintegrated red corpuscles. Levaditi, and Neisser and Wechsberg have described, as the result of intravenous injections of *Staphylococcus aureus*, areas of coagulative necrosis in the rabbit's kndney, which they attribute to thrombi composed of disintegegrated leucocytes caused by the staphylococcus leucocidin, to which I have already referred.

I have dwelt at some length, although of necessity incompletely, upon the bacterial hemolysins, leucocidins and hemagglutinins, because we are better informed about these agents than concerning other members of this recently recognized class of bacterial toxins. I have already expressed the opinion that similar poisons acting specifically upon other cells of the body are produced by bacteria; indeed, neurotoxins and nephrotoxins of this type have been reported. The difficulties in the way of direct proof of the existence of these other bacterial cytotoxins are greater than in the case of those acting upon the red and the white blood-corpuscles, but doubtless they can be overcome. Of course we have evidence of the action of bacterial poisons upon various body-cells, but this is not enough. At present we can apply only in a vague and unsatisfactory way to the explanation of pathological processes most of the knowledge of this kind which we possess. What is urgently needed is a separation of these poisons and a determination of their source, constitution, mode of action, and degree of specificity along such lines as have been followed so fruitfully in the investigation of the soluble diphtheria and tetanus toxins, these other toxins of bacteria and of venom already considered, and the cytotoxins of normal and of immune serum. The path leading apparently in the right direction has already been opened and, if I mistake not, its further pursuit is most promising of valuable results in the near future.

Consider by way of illustration how helpless we now are in our efforts to explain the characteristic lesions of typhoid fever on the basis of our knowledge of the properties of the typhoid bacillus. That these lesions are referable to the action of toxins cannot, I think, be seriously questioned. Especially from the investigations of Mallory we know that the most characteristic histological changes of this disease consist in the proliferation of the reticular or so-called endothelial cells of the lymphatic tissue of the intestine and the mesenteric glands and of similar cells in the splenic pulp, and in the assumption by these proliferated cells of remarkable phagocytic activities toward the lymphocytes in the former situations and toward the red corpuscles in the spleen. Mallory believes that these changes are best interpreted by supposing that the typhoid toxin directly stimulates to proliferation the endothelial cells, which then devour their offspring, the lymphocytes, and the red corpuscles. I have suggested as another explanation that the typhoid bacillus produces a lymphocytotoxin and an hemolysin, and that the proliferation of the fixed cells is partly compensatory and partly for the increased production of macrophages. We already know that this bacillus generates a hemolytic agent, and we also know that one of the effects of injection of hemolysins is to increase greatly the number of macrophages containing red corpuscles in the spleen. Through the kindness of Professor Flexner I have had the opportunity of studying the extraordinary changes produced in all the lymphatic glands and in the bone-marrow of rabbits by injections of lymphotoxic or myelotoxic serum obtained by treating a goose with lymphatic or marrow tissue of the rabbit. One of the most striking effects of this poison for lymphocytes and other leucocytes is the very extensive proliferation of the reticulum-cells in the lymphatic nodes and of the marrow-cells. In the light of these observations it is clear that a positive demonstration of the production of a lymphotoxin by the typhoid bacillus would materially advance our understanding of the morbid anatomy of typhoid fever. Another lesion of this disease only second in importance to those mentioned is the occurrence of plugging of the small vessels. Dr. Fisher in my laboratory has recently shown that such thromboses are produced by the experimental inoculation of rabbits with the typhoid bacillus. I have already pointed out that many of these plugs are agglutinative thrombi.

Of course infectious diseases other than typhoid fever could also be cited, did time permit, as equally forcible illustrations of the aid which pathology may reasonably expect from more precise knowledge of the bacterial cellular poisons. It is probable that such knowledge will lead to improvements in the quality for therapeutical purposes of the so-called bacteriolytic sera, some of which, as now prepared, are not wholly devoid of antitoxic properties as is often represented. We may also anticipate from investigations of the character indicated much light upon one of the most puzzling of bacteriological problems, the localization of bacteria in disease. Toxic lesions and the plugging of small blood-vessels are certainly often of decisive influence in determining this localization, as has been demonstrated especially for the staphylococcus pyemias by Muscatello and Ottaviano.*

The toxins to which I have chiefly directed your attention in this lecture are those produced by bacteria. But, as already pointed out, we now know that the animal body has the power to produce specific poisons directed not only against

*Muscatello and Ottaviano. Virchow's Archiv, 1901, CLXVI, p. 212.

invading bacterial cells but also against all sorts of foreign cells. Following the discovery by Belfanti and Carbone in 1898 of this capacity in relation to injections of blood a wholly new domain of biology has been opened to experimental research. Attention has been withdrawn for the moment to a considerable extent from the bacterial toxins and concentrated upon the animal cytotoxins. Here new facts and conceptions of absorbing interests have been disclosed in an abundance and with a rapidity which are simply bewildering.

It was my original design to include in this lecture a consideration in some detail of these animal cytotoxins, but so much time has been occupied with other aspects of the subject that I am compelled to abandon this intention. This is perhaps less to be regretted inasmuch as I understand the main purpose of these lectures to be the presentation of applications to medicine and surgery of scientific discovery, and it is precisely this side of the recent work on animal cytotoxins which seems to me in the main not yet ripe for profitable discussion on this occasion. It is true that facts of much scientific and practical interest have been discovered by the investigations, initiated by Shattock and by Greenbaum, followed by Landsteiner, Ascoli, Eisenberg, Kraus and Ludwig, and others, concerning the isoagglutinative and isolytic properties of human sera in health and in disease. But the really great practical questions in this domain relate to the production of autocytotoxins in the human and animal body. What is the nature of that very efficient regulatory mechanism underlying the horror autotoxicus (Ehrlich) which prevents either the action or the formation of autocytotoxins in consequence of absorption of our own degenerated and dead cells? Can this protective mechanism be overthrown by pathological states and self-generated cellular poisons become operative in the causation of anemias, hemoglobinurias, chronic interstitial inflammations, uremia, eclampsia, epilepsy, and other diseases? To these and similar important questions the existing experimental data seem to me too insufficient and inconclusive to furnish any decisive answer at present. I share, however, the hope and belief of many that there is a field for exploration which, although surrounded with many difficulties, gives promise of discoveries of a far-reaching and important nature. I anticipate that some future Huxley lecturer will find in this realm a fascinating theme.

In this connection may be mentioned the great pathological interest pertaining to the recent investigations of Jacoby, Conradi and others on the phenomena of self-digestion or autolysis of inflammatory exudates and necrotic material within the living body. One can readily convince himself of the energetic action of autolytic ferments by the simple experiment of placing a piece of fresh pneumonic lung in the stage of gray hepatization under chloroform and noting the rapid solution of the exudate, in contrast with the absence of this process in earlier stages of the disease. Conradi finds that bactericidal substances, to which he attaches much importance, are produced in tissues and cellular exudates undergoing autolysis.

Although my theme relates especially to the bearing of studies of immunity on pathology, it is hardly necessary to say that these studies were primarily undertaken to elucidate the great problems of predisposition and resistance to disease and that in this field they have borne their richest fruits. It is especially gratifying to note the close convergence of the two doctrines of immunity, the cellular and the humoral, brought about by these recent discoveries. On the one hand, the phagocytic school, represented so brilliantly by Metchnikoff and his coworkers in the Pasteur Institute, recognize and apply to the fullest extent in the explanation of acquired immunity the cytolytic principles based upon the cooperative action of intermediary bodies and complements. On the other hand, the humoral school, led by our German confrères, which has been so fruitful in results of the greatest scientific and practical value, recognize the cells, and especially the leucocytes and other cells of the blood-forming organs, as the immediate source of the protective substances. There are many differences in details, especially in terminology and in interpretation, which makes the divergence seem greater than it really is. The essential difference between the two schools concerns the place where the two forces, intermediary body and complement, unite. All are agreed that the intermediary body exists free in the blood-plasma, but Metchnikoff strenuously insists, especially on the basis of Gengon's experiments, that the complement or cytase is within the leucocytes, from which it is not secreted, but can be liberated only through damage to these cells. This question certainly needs further investigation before it can be regarded as settled. The recent recognition and complements through researches made in Ehrlich's laboratory marks a still closer approximation of the two schools.

The deeper insight which we have recently gained into the nature of the forces concerned in immunity makes especially desirable the systematic study of the blood and other fluids of human beings in health and in disease with reference to their content of specific anti-bodies, particularly of the bactericidal substances. It can scarcely be doubted that knowledge of this kind will be in various ways of practical value to the physician and surgeon. The simplest procedure, and the one hitherto generally adopted, is the estimation of the bactericidal power of the blood-serum in toto. For this purpose Professor Wright* has devised an ingenious method which in his hands has furnished extremely interesting information concerning variations in the bactericidal power of the blood as regards the typhoid bacillus in health, under the influence of fatigue, in the

*A. E. Wright, Lancet, 1898, I., p. 95; 1900, II., p. 1536; 1901, I., pp. 609 and 1532; and 1901, II., p. 715.

course of typhoid fever and after antityphoid inoculations. The older methods, however, while not without value, do not inform us of the total content of the blood in immunizing substances, and have led to very discordant results, particularly as to the influence of infection upon the bactericidal power. Thus Conradi* finds, in opposition to most previous experimenters as well as to the later results of Wilde, that infection with the anthrax bacillus does not at any stage influence materially the bactericidal properties of the blood.

A useful and readily applicable method for the determination separately of the intermediary bodies and of the complements of human serum is urgently needed. When one takes into consideration the plurality of complements and of intermediary bodies, the fallacies of interpretation which may arise from failure to take account of anticomplements, of anti-immune bodies, of complements, of amboceptoids, of deviation (Ablenkung) of complements, and other principles in this complicated subject, it is clear that the problem is not an easy one.

Notwithstanding these difficulties work has already begun along these new lines and has led to interesting results. We know that the content of the blood in specific anti-bodies, and especially in complements, varies in significant ways under diverse conditions, as in infancy and in adult life, in health, in different states of nutrition, under the influence of fatigue, of inanition, of pain, of interference with respiration, of alcohol, and in disease. The infant comes into the world with protective anti-bodies in its blood smaller in amount and less energetic than those possessed by the healthy adult. It is an important function of the mother to transfer to the suckling through her milk-immunizing bodies, and the infant's stomach has the capacity, which is afterward lost, of absorbing these substances in an active state. The relative richness of the suckling's blood in protective anti-bodies, as contrasted with the artificially fed infant, explains the greater freedom of the former from infectious diseases.

The important question of the influence of preexistent disease in predisposing to infection has been brought nearer to a solution by recent studies of immunity. Schutze and Scheller† have demonstrated that while the normal rabbit promptly regenerates the complements used up in consequence of the injection of hemolytic serum, a rabbit infected with the hog-cholera bacillus has lost this capacity. My former pupil, Dr. Longcope, has kindly placed at my disposal the unpublished results of an investigation which he is making under Professor Flexner's direction at the Pennsylvania Hospital of the intermediary bodies and the complements in human blood in different diseases. Colon and typhoid bacilli are used as the tests, as, unless one accepts Bordet's doctrine of the study of complements, it is more important for the study of problems of infection to determine bacteriolytic than hemolytic anti-bodies. One of the earliest results of the systematic bacteriological examinations which we make at all autopsies at the Johns Hopkins Hospital was the recognition of the great frequency of terminal infections, formerly often undetected by the clinician, in chronic diseases, particularly of the heart, the blood-vessels, and the kidneys. Dr. Longcope finds, although not regularly, still in many cases of these diseases, a marked reduction in the quantity of complements, which may amount to a total loss of the colon complements. The analysis of the cases brings out unmistakably a definite relation between this loss of complement and the predisposition to infection. The study of a series of acute infections, chiefly of a surgical nature, shows that in the course of the infection complements are being constantly used up and regenerated, and that at any given time there may be an excess or a reduction of the bacteriolytic power of the blood. Thus far it has been found impossible in these acute infections to attach any prognostic significance to the amount of complement or of bacteriolytic power, nor could any definite relation be determined between the leucocyte count and the content of complements.

Although we have traversed, Gentlemen, in this lecture a path which I fear has seemed to you a long and winding one, I am conscious that I have been able to point out the features of the prospect only imperfectly and incompletely. The extent and the richness in details have been embarrassing. I trust, however, that I have been able to indicate in some measure the great interest and importance to biology, to physiology, to pathology, to every department of medical science and art of investigations which have led to a deeper insight into certain manifestations of cellular life. What has been conquered by these investigations is simply a bit of new territory pertaining to the intimate life of the cells, and we find here, as whenever we are able to penetrate deeper into this life, that there comes a flood of new light into every department of biology. The researches on immunity, which to some of short vision once seemed to threaten the foundations of cellular pathology, have served only to strengthen them. These researches, which have already led to the saving of thousands of human lives, and will lead to the saving of untold thousands more, have been carried on by the experimental method, and can be conducted in no other

*Conradi. Zeitschr. f. Hygiene, 1900, XXXIV., p. 185; 1901, XXXVIII., p. 411.
† Schutze and Scheller. Zeitschr. f. Hygiene, 1901, XXXVI, pp. 370 and 459.

way. This method is as essential for the advancement of medical science as for that of any of the natural or physical sciences. To restrict unnecessarily and unjustifiably its use is nothing short of a crime against humanity. It is an evidence of the robust vitality of English physiology and medicine that in spite of unwarrantable obstacles thrown in their path their contributions to science in recent years have been so numerous and so important. The influence of English thought and action is great with us in America. See to it, my colleagues and men of science in England, that you retain for yourselves and hand down to your successors, at least without further impairment, the means of promoting medical knowledge and thus of benefiting mankind.

## ORIGINAL ARTICLES.

### DRUG HABIT: REVIEW OF ARTICLES BY DRS. HARE AND LOTT.*

BY GEO. E. PETTEY, M.D.,
OF MEMPHIS, TENN.:

Two articles have recently appeared in medical literature that deserve particular attention and invite some criticism. One, from the gifted pen of Dr. H. A. Hare of Philadelphia, is entitled "A New Method of Treating the Morphine and Alcohol Habits," and was published in the MEDICAL NEWS of June 7. The other, treating of "The Drug Habit and Its Cure Without Pain," is by Dr. M. K. Lott of Cameron, Texas. This was published in the Therapeutic Gazette for February, 1902. These articles are both on the use of hyoscine in the treatment of drug and liquor addictions, and are valuable contributions to our literature. At the same time they contain certain statements which, to say nothing worse, are likely to impair their usefulness.

Dr. Lott reports the treatment of a series of cases of morphine and whiskey habit with hyoscine; and Dr. Hare says, "I have tried this plan in six cases with extraordinary results from the following points of view: First, the patient can take massive doses (of hyoscine) for days at a time, as much as one-fourth of a grain each day hypodermatically, with no evil effect on any vital function; second, they suffer very little, if at all, from the immediate withdrawal of morphine, and third, and more surprising, the desire for the drug is largely, if not entirely, dissipated after a few days."

I can confirm the second and third of these statements, but the first is so broad and sweeping that it should not go without challenge, since, if it were followed, it would inevitably result disastrously, and soon bring a most valuable plan of treatment into disrepute, if not into round condemnation. It is unfortunate that such a statement should have been made by one occupying the position and speaking with the authority of Dr. Hare.

One-fourth of a grain of hyoscine administered in 24 hours is a little more than one one-hundredth of a grain each hour. I have had quite an extensive experience with this drug and have watched its effects very closely. Within the last four years I have treated 350 cases of drug and liquor addictions with hyoscine as the principal active agent; and basing an opinion upon that experience, I am prepared to say that there are as many people who can not safely take one one-hundredth of a grain of hyoscine every hour for days at a time as there are who can with safety take that quantity, and that such dosage, routinely administered, as advised by these gentlemen, would frequently prove fatal. I know of no other drug whose effects vary so greatly with different individuals as do those of hyoscine, none that requires such close and discriminating care in its administration. To illustrate the wide difference in the effects of this drug on different individuals, and to show that its prolonged administration in the treatment of morphinism is not necessary, I will give the clinical notes of a few cases.

Mrs. B., aged fifty-two years, weight 140 pounds, had a morphine habit of 15 years' standing. Her daily quantity was 10 grains taken by mouth in two doses. She came for treatment October 9, 1899. The usual dose of morphine was given at 3 P.M. Patient received a Turkish bath, was deprived of her supply of morphine, and placed in room specially prepared for her with a trained nurse in constant attendance. From 4 to 10 P.M. purgative course of calomel, cascara, strychnia and ipecac was given. The next morning this was followed by a full dose of castor oil, and later by a bottle of citrate of magnesia, from which the bowels were thoroughly empty by 10 A.M. The bowels having acted freely, there was no demand for morphine until 2 P.M., at which time she said she was nervous and aching and wanted her dose. At that time her pulse was 65, full and regular; respiration 18; skin moist, but not sweating. At 2 P.M. I gave one one-hundredth of a grain of hyoscine, repeating the dose at 3 and at 4 P.M. I then left the patient, expecting to return in two hours, but shortly before that time had expired I was hastily called to see her. I found her profoundly narcotized, breathing stertorously 8 to 12 per minute, with lower jaw dropped, skin bathed in perspiration, pulse 40 to 50 and irregular. She could not be aroused to any degree of consciousness.

The administration of restoratives, such as caffein, strychnia, nitroglycerin, hot applications to spine, etc., was at once begun, and was continued for three hours. At times there seemed to be some improvement, but soon these signs would

* Read before the Tri-State Medical Society of Georgia, Alabama and Tennessee, at Birmingham, Alabama, October, 1902.

disappear, and at the end of the third hour of these efforts her condition was decidedly more hazardous. Patient very much cyanosed; breathing more irregular and only from six to eight per minute; pulse more irregular and of less volume. At times responding to the stimulants, the pulse would run up to 60 or 70 to the minute, and would then drop back to a much slower rate, at one time being as low as 38 per minute. It seemed that all remedies at hand were failing, and that my patient would soon die in spite of all efforts to save her. The excessive diaphoresis and failing pulse-volume caused me to think of the possible efficiency of saline solution. I injected one quart of normal salt solution into the cellular tissues, and the same quantity into the bowel with a long colon tube. In less than 30 minutes there were distinct signs of improvement; within an hour her breathing was fairly good, 12 to the minute; cyanosis had disappeared; pulse was 50 and of fair volume; sweating less profuse, and the extreme prostration had given way to a condition of fair tone. Her condition gradually became more normal. In three hours from the time the first salt solution was given it was repeated, and she was allowed to continue to sleep without efforts to arouse her. From this time on her condition was satisfactory; sleep was a little more profound than natural, but respiration and circulation were good. Sixteen hours from the time the last dose of hyoscine was given she awoke voluntarily, but was languid and drowsy for several hours more. At the end of this time she began to complain of pain in her back and limbs. I gave her one two-hundredth of a grain of hyoscine and repeated the dose in 30 minutes. This gave relief which continued for a period of six hours, when the limbs were again uncomfortable. She said she had no desire for morphine but would like to have something to stop the aching in her legs. I gave one one hundred and fiftieth of a grain of hyoscine, which brought complete relief, and when the effects of this had subsided the pain did not return. Not another dose of medicine of any kind was given in the case. She had no desire for morphine or any other stimulant, but expressed herself as feeling well and desired something to eat. Liquid nourishment was given and retained, and within three days she was eating heartily and said she enjoyed her food more than she ever had done before. At that time the most remarkable feature of this case to me was the fact that she could sleep from five to seven hours every night and then frequently take a nap of an hour or more during the day. She made an uneventful and rapid recovery, gained 30 pounds in flesh in four months, and has remained free from the morphine habit from that day to this. Her husband says that instead of her former sedentary and seclusive habits she now wants to be up and going all the time, and would not willingly take a dose of morphine even to save her own life.

There is little doubt that this patient would have died from the effects of the three one-hundredth grain doses of hyoscine given her had it not been for the happy effect of the normal salt solution. It evidently saved her life by increasing the volume of the circulating medium and by rendering less concentrated the narcotic poison it held.

I have had quite a number of cases that were extremely sensitive to the effects of hyoscine, but the following case shows about as marked intolerance as any: Mrs. E. D., aged thirty years, blonde, weight 125 pounds, had a morphine habit of 13 years' standing, her daily quantity being 20 grains taken hypodermatically in three doses. From 4 to 10 P.M., July 27, 1901, a mercurial and vegetable cathartic was administered, also a vapor bath. The last morphine, seven grains, was allowed at 6 P.M. At 7 o'clock the following morning two ounces of castor oil was given, followed two hours later by a bottle of citrate of magnesia. The bowels began to act at 5 A.M., and between that time and noon six free evacuations occurred. Patient was fairly comfortable during the time, and did not ask for her drug until noon. At 12.25 P.M. I gave one one-hundred and fiftieth of a grain of hyoscine and one grain of sparteine. In 30 minutes the patient was asleep, and she slept an hour. Face was deeply flushed; respiration and circulation slightly accelerated. She awoke at 2 P.M., when her mind was clear. Then she complained of aching of limbs. At two P.M. I gave one two-hundredths of a grain of hyoscine, after which she fell asleep again, and slept about an hour. On waking, her mind was wandering, and she continued in a mild loquacious delirium until 6 P.M., when the mind began to clear, and as consciousness returned she said she was uncomfortable. At 9 P.M. I again gave one one hundred and fiftieth of a grain of hyoscine. Delirium was fully reestablished in 30 minutes, and for several hours it was of a more marked type, continuing without material abatement until 6.30 A.M. At that time she was in a measure conscious, complained of some discomfort, and said she would take morphine if she had it.

At 7 A.M., July 29, one two-hundredth of a grain of hyoscine and one grain of sparteine were given. Delirium recurred in a short time, continuing without any sign of abatement during the entire day, and even the next morning, twenty-four hours after the last dose of hyoscine had been given her mind was not entirely clear. During this time, although she had some lucid moments, she did not complain of any pain or discomfort whatever, and said she had no desire for morphine. No medicines of any kind were given her. During this day, July 30, the fourth from the beginning of treatment, she took liquid nourishment, suffered no pain or even discomfort, showed no abstinence symptoms of any kind, and while she said she felt weak, she had no desire for morphine. She was given a bath morning and evening, sat up most of the day, and slept between four and five hours that night without medicine of any kind, nor did she

sleep less than that any night thereafter. I kept her with me three weeks. By the end of the first week her appetite was ravenous; she could eat anything she was allowed with impunity; had no diarrhea or other complication, and gained flesh at the rate of half a pound a day. At the end of the third week she was discharged in almost perfect health, looked like an entirely different woman, and at no time had she any desire for morphine, nor did she show any inclination to take other stimulants.

This case is remarkable because of the extremely small quantity of hyoscine required to bring the patient well under its influence, and for the length of time the effects of the drug continued. This patient would most likely have been made violently delirious, and probably thrown into convulsions, from cerebral congestion, or have been dangerously narcotized, by the administration of one one-hundredth of a grain of hyoscine every hour for even three or four hours in succession, not to speak of several days.

These two cases show the marked susceptibility of some people for hyoscine, and that the routine or careless administration of that drug is an extremely hazardous procedure. Ther are others who have an unnatural tolerance for this drug. The following case shows remarkable tolerance: Mrs. T. N., a blonde, aged twenty-five years, weight 120 pounds, five feet four inches in height, compactly built, was of a sensitive, nervous temperament. Her morphine habit was of four years' standing, and the daily quantity taken was 10 grains, hypodermatically, in four or five doses.

March 2, 1902, 4 to 10 P.M. Active purgative course of calomel, cascara, strychnia and ipecac. Last morphine, two and one half grains, at 9 P.M. Vapor bath.

March 3, 5 A.M. Bottle citrate magnesia. 7 A.M.—Bowels have acted several times, but character of actions not altogether satisfactory. Is suffering and wants morphine. 7 A.M.—Gave 1-200 grain hyoscine. 7.30 A.M.—Gave 1-200 grain hyoscine. 8 A.M.—Gave 1-100 grain hyoscine. 9 A.M.—No perceptible effect from doses given. 9 A.M.—Gave 1-75 grain hyoscine. 9.30 A.M.—Gave 1-50 grain hyoscine. 10 A.M.—Very little effect from preceding doses. Mouth slightly dry; is still suffering. 10 A.M.—Gave 1-50 grain hyoscine. 11 A.M.—Gave 1-50 grain hyoscine. Slept two hours; face flushed; mind clear; pulse and respiration slightly accelerated. 2 P.M.—Gave 1-25 grain hyoscine. Slept three hours; comfortable. 5.50 P.M.—Gave 1-25 grain hyoscine. 7 P.M.—Gave 1-50 grain hyoscine. Uncomfortable. 9 P.M.—Gave 1-25 grain hyoscine. 12 P.M.—Gave 1-25 grain hyoscine.

March 4, 4 A.M.—Gave 1-25 grain hyoscine. 7 A.M.—Gave 1-50 grain hyoscine. 7.45 A.M.—Gave 1-25 grain hyoscine. 8.30.—Gave 1-25 grain hyoscine. From 5.50 P.M. to 8.30 A.M. was quiet but not entirely comfortable, sleeping at intervals, mind clear up to 9 A.M. From 9 A.M. to noon mind wandered slightly, a very mild delirium, but at other times was entirely clear. Did not complain of discomfort until 1 P.M. 1 P.M.—Gave 1-25 grain hyoscine. Quiet and comfortable till 8 P.M. 8 P.M.—Gave 1-25 grain hyoscine. Nauseated. 9 P.M.—Gave 1-25 grain hyoscine. Slept two hours.

March 5, 1 A.M.—Gave 1-20 grain hyoscine. Slept three hours, and on waking mind was clear. Was comfortable; pulse 60, good volume; respiration 20; temperature normal; skin moist. Craved lemonade and buttermilk, which were given but vomited after an hour or so, and nausea continued most of the day. Vomited matter was green and offensive. As the day advanced she became more nervous and uncomfortable. The bowels not having acted for 36 hours, and not very satisfactorily at the beginning of treatment, 30 grains of hyposulphite of soda was given, and repeated every hour for four hours. The bowels then began to act, and a number of free bilious actions occurred. Nausea then ceased; there was no further marked discomfort in the case, and she made an uninterrupted recovery, never at any time expressing any desire for morphine, nor was that or any other medicine given. The bowels acted two or three times during each 24 hours, but no diarrhea or other complication occurred. She did not sleep more than two or three hours at night for the first few nights, but gradually improved in that respect until at the end of 10 days she was sleeping five to six hours out of the 24 daily.

I know no explanation of this patient's extreme tolerance for hyoscine. She had never taken hyoscine or any drug of that class with her morphine. She had been treated about a year before she came to me for the morphine habit. She told me that the physician who treated her said he had given her very large doses of hyoscine but was never able to bring her under its influence sufficiently to keep her from suffering, and for that reason the treatment was abandoned and the habit resumed.

I have had one other case that showed as great or even greater tolerance for hyoscine than this one; but that patient had been taking an advertised "cure" for the morphine habit for several months, and I have reason to believe that one of its ingredients was hyoscine. Large doses of hyoscine had no perceptible effect on him, and after trying them until I was fully satisfied that he was a hyoscine habitué, a different line of treatment was adopted, to which he responded normally.

In the sixth case reported by Dr. Hare, he says that 10 days after the beginning of treatment "the patient, while still receiving these massive doses of hyoscine, began to pass from under their influence, her tongue was moist, her mind clear," etc. It is evident that in this case the morphine habit had been supplanted by the hyoscine habit. This patient was still receiving doses of this drug when the case was reported. From the course pursued in the first case reported by him, I presume that this drug is to be discontinued by grad-

ual withdrawal. In this connection I wish to enter a protest against such a procedure, and to remind the profession that there is nothing in this condition or in the nature of this drug to warrant the belief that the method of gradual reduction would be more successful as a treatment for the hyoscine habit than it has been for the morphine habit, in which it has been proved to be a stupendous failure. If the example of Dr. Hare in giving hyoscine two weeks or longer until tolerance for it is established is followed, the hyoscine habit will soon be another curse with which unfortunate victims will have to contend. There is no reason whatever for the administration of hyoscine in a morphine case for a longer period than two to four days, so far as the cure of that habit is concerned. Forty-eight hours should be the extreme limit as a rule, and that is longer than is necessary in most cases.

In an article published in the last October number of the Therapeutic Gazette I contended for the following propositions:

That abstinence symptoms, or the various manifestations thus designated, which occur upon the withdrawal of morphine, are due mainly to auto-intoxication from effete material locked up in the system by the effects of morphine, and to the secondary effect of that drug; that when a primary step in the treatment is thorough elimination of both the stored-up drug and the effete material with which these patients are surcharged, the most distressing and dangerous symptoms met upon withdrawal are avoided; that if the system is thoroughly freed from effete material, and morphine discontinued, all distressing painful symptoms subside within three days—as soon as the secondary effects of morphine are exhausted—*without treatment of any kind;* and that the essential office of hyoscine in the treatment of this habit is to keep the patient from suffering *during that interval;* that as a rule all medication can and should be discontinued within four or five days.

Dr. Hare ignores these contentions altogether, and Dr. Lott takes a different position. He says: "In treating for opium or any of its preparations, there should be nothing given to cause the bowels to move, for as soon as the morphine is out of him, during the second day, a bilious diarrhea will set in that will worry the patient a good deal." Thus, he waits for the system, released from the benumbing influence of morphine, to awake to the presence of the large accumulation of excrementitious matter and set up a diarrhea to throw it off, and allows this to occur when the patient, recently deprived of the sustaining power of morphine, is least able to bear such a drain.

But let us see what are some of the other results these gentlemen get from the treatment as they give it, and how long they are about it.

Dr. Hare says of his first case: "In this particular case the large doses of hyoscine were continued for a period of over two weeks and then were gradually decreased. It is now several months since the treatment ceased," and "I have seen this patient's physician during the last few days, and he tells me that not only is the man not taking morphine, but that he seems to be improved in every way, and has gained 10 or 12 pounds in weight." An average patient, whose system is put in proper condition at the beginning of treatment, and to whom only what hyoscine and other medicine he needs is given, will gain flesh at the rate of one-half to one pound per day until his full normal weight has been reached, and his improvement in every other respect will be so marked that it will not be left to the physician merely to state that he "seems to be improved."

In Dr. Hare's last case he says: "Twelve days after treatment began she asked for solid food." A patient of this class, whose system has been properly cleansed of effete material and relieved from the effects of auto-intoxication at the beginning of treatment, will usually crave solid food on the fourth or fifth day thereafter, and by the end of the first week will have an appetite that would do credit to a field-hand.

Of his patient, at the end of the period during which he gives hyoscine, Dr. Lott says: "Thus far all is well; the patient has been relieved from the drug, but he is not cured; it will take a long time before his cure is completed, and often his courage and his fortitude will be taxed to the utmost. True, he has escaped from morphine without pain, but he will not be able to rebuild the shattered constitution without more or less suffering. The functions of the body so necessary to health have been impaired; appetite, digestion, assimilation, sleep, a proper equipoise of the nervous system are to be regained. Not only so, but often for the first week, or, for that matter, for the first month, there is pain in the back and knees, feet and arms, sometimes quite severe." What? Did you not say that the patient had escaped from morphine without pain? Is it possible that while he was thus escaping some other blighting disease fastened itself upon him and is causing all this suffering? Or can all this pain and discomfort be a necessary part of the reconstructive process that lies before him? Is the reconstructive process a painful one? Not so; but with all charity I must say that the marked discomfort of this patient is mainly due to the neglect by his physician of one of the fundamental doctrines of medical science; that is, that retained excrementitious matter greatly aggravates and intensifies any disease to which the human economy is liable, and that its removal is properly the first and often the most essential step in treatment.

The use of morphine interferes with the proper working of all the excretory glands, and causes prolonged retention of the products of waste, resulting in profound auto-intoxication. The effects of this are so manifold and far-reaching that it is almost beyond human ability to enumerate them. Suffice it to say that all the annoying and painful symptoms with which Dr. Lott says his patients have to contend are daily met with and well understood to be the effects of

auto-intoxication. It is also axiomatical that if the system is not too profoundly impressed nature will finally come to the rescue, and set up a diarrhea or other discharge to relieve the victim of this poisonous matter. If nature is better prepared to do this unaided and alone than by the addition of purgatives, diuretics, diaphoretics, etc., skilfully administered, then indeed have the fathers of medicine striven in vain to establish our art. Yet notwithstanding the fundamental teachings, and notwithstanding that Dr. Lott recognizes the fact that the system of his patient is in a condition in which a diarrhea will soon be set up to clear it of offensive excreta, he advises that no purgative be given at the beginning of treatment, but waits to give nature a chance to do that work without assistance. This is certainly a strange doctrine, and yet here we have an eminent professor of materia medica indorsing it.

It does seem strange that in this age of the world it should be necessary for any one to insist that as a primary step in the treatment of any disease the system should be cleansed as fully as possible of all retained excreta and other noxious matter. The universally recognized value of purgatives depends upon the fact that with their aid the system can be more readily, perfectly and economically cleansed of retained excreta or other offensive matter than it can be by a diarrhea set up by the irritating action of these substances. Diarrhea, thus induced, often runs a protracted course, and if the purpose of nature is ultimately accomplished without artificial aid it is by the most profligate expenditure of the patient's strength and other resources. In Dr. Lott's cases, nothing so retards their recovery or shatters their constitutions as does the diarrhea.

In the old methods of treatment, in which withdrawal of the drug was attempted without preceding elimination, diarrhea was one of the most trying and difficult complications to meet, and that which most often caused a return to the opiate. Since this diarrhea can be prevented altogether by a well-directed eliminating course given at the beginning of treatment, and since this can be given without discomfort, and when the patient is still under the sustaining influence of morphine, why should it not be given? Not only does elimination prevent the diarrhea, but it gives many other advantages. For one thing, it shortens the time during which it is necessary to give hyoscine or any other medicines. The patient, freed from irritating excrementitious matter, is far more comfortable, and has no such array of painful symptoms to contend with as Dr. Lott describes.

In order to show the contrast between a case treated with thorough elimination as the primary step and those reported by these gentlemen, I will give the clinical notes of a case.

Dr. F. C., aged thirty-three years, weight 150 pounds, nervous temperament, began the use of morphine in 1898, and gradually increased the quantity to 10 grains a day. In August, 1899, cocaine was added, and at the time of beginning treatment he was taking about 10 grains of each daily, divided into 10 to 15 hypodermatic doses. He was rarely able to get to sleep before 2 A.M., because of the exciting effects of cocaine, which was used up to about 9 P.M. and then discontinued until morning. He came for treatment January 9, 1900.

January 9.—Gave a capsule containing two grains of calomel, two grains powdered extract cascara, one-eighth of a grain strychnia and one-fourth of a grain ipecac, at 4, 6, 8, and 10 P.M. The usual doses of morphine and cocaine were allowed until 9 P.M., and then discontinued. At this hour the patient received a Turkish bath.

January 10.—Had a very copious action from bowels at 5 A.M., and another at 6.15 A.M. At 7 A.M. gave three ounces of castor oil, and between that time and 10 A.M. had five free bilious actions from bowels. No nausea or other distress attended the action of bowels. 11.30 A.M.—Is suffering and wants morphine. 12 M.—Gave 1-200 grain hyoscine. 12.15 P.M.—Gave 1-200 grain hyoscine. 12.45 P.M.—Gave 1-150 grain hyoscine. Slept three and a half hours. 5.25 P.M.—Gave 1-150 grain hyoscine. Slept three hours, mind clear. 9.00 P.M.—Gave 1-150 grain hyoscine. Suffering. 9.20 P.M.—1-150 grain hyoscine. 9.40 P.M.—1-150 grain hyoscine. Slept three hours; on waking mind is still clear.

January 11.—1.15 A.M.—Gave 1-150 grain hyoscine. Suffering. 3.15 A.M.—Gave 1-150 grain hyoscine. More comfortable. 5.45 A.M.—Gave 1-150 grain hyoscine. Mind still clear. 6.20 A.M.—Gave 1-100 grain hyoscine. 8.40 A.M.—Gave 1-100 grain hyoscine. Comfortable. 10.40 A.M.—Gave 1-100 grain hyoscine. Mild delirium. 12.15 P.M.—Gave 1-150 grain hyoscine. 3.00 P.M.—Gave 1-150 grain hyoscine. Hyoscine discontinued. Delirium of mild type continued to 9 P.M., at which time the mind was about clear. Comfortable. 11.00 P.M.—Gave 20 grains of trional. Slept three hours.

January 12.—9 A.M.—Legs and back aching; temperature 99° F. Gave five grains each of quinine and antikamnia at 9 A.M., 12 M. and at 3 and 6 P.M., but no other medicine. 8.00 P.M.—Aching of legs and back relieved. Comfortable. 9.00 P.M.—Gave 20 grains of trional.

January 13.—9.00 A.M.—Slept some last night, and rested quietly during the remainder of night. Ate breakfast with relish.

January 14.—Spent a comfortable day and night without medicine.

January 18.—The patient has taken no medicine in last five days and nights; feels weak, but does not suffer in any way; has no desire for morphine or cocaine, but on the contrary feels that their effects would be decidedly unpleasant to him now; eats heartily, goes to bed early, sleeps soundly all night, and says he feels like a new man. Is supremely happy since he realizes that he is no longer a drug-slave. Placed in charge of wife and sent home.

January 25.—At this date the condition of the patient may be judged by what his wife wrote to me: "Doctor is doing nicely. If he improves in

the next month as he has this week you will not know him. He sleeps well at night, gets up at 7 o'clock every morning, and seems perfectly comfortable. It seems so strange to see him up early every morning now, for when he was taking drugs he could hardly be gotten out of bed before noon. He is eating heartily, and everything seems to agree with him. His bowels have not given him any trouble at all. He says he has no desire for morphine or cocaine, and that he rarely thinks of them now. He left this morning for a week's hunt on the lakes."

January 30.—Patient visited me at my office. He has gained 15 pounds in weight, and looks like a different man. He feels a return of his old time energy, and is going to make up for lost time.

This case is fairly typical of a large percentage of those treated by the method I advocate, with the possible exception that this patient, being a morphine and cocaine habitué, regained his normal capacity for sleeping a little earlier than patients do who have not been taking cocaine. There is certainly no such protracted painful convalescence, as Dr. Lott says his patients have. He attributes these painful symptoms to the presence of morphine in the system, but in this he is in error. Morphine in the system is not "the malady," and is not so much to be contended with as the effete material which it imprisons therein. Another statement by Dr. Lott that should be taken with some degree of allowance is this: "Remember that hyoscine antidotes morphine and morphine antidotes hyoscine. If the patient gets too much of one, give the other." This statement is entirely too broad. It is well understood that hyoscine, and the entire belladonna series are physiologically antagonistic to morphine in a part of their range of action, but it is equally well established that in other respects they are synergistic. There is certainly no chemical antagonism between them, therefore to say that they antidote one another is misleading. They are both hypnotic, both anodyne, and both narcotic and in these particulars they are synergistic. It certainly would not have been admissible to give the patient I have reported first in this article morphine because she had too much hyoscine. She was already profoundly narcotized, and morphine would have intensified that narcosis. I have no doubt that many cases of morphine poisoning are lost because of the too free administration of belladonna with the idea that it is an antidote. It certainly does not deserve to be so classed, and neither does hyoscine. In some respects and to a limited degree they oppose each other, but that is as much as can be safely said.

In my article referred to above I said: "Hyoscine does not materially affect the vital functions, or leave after-effects on either the mind or body of the patient, therefore it should be given until its full physiological effects are manifested if necessary." But I also said: "The administration of this agent should not be left to a nurse, but the physician should remain with the patient in person. The dosage in one case is no index to what will be required in the next. Only by the physician being present and personally observing the effects of each dose can the proper dosage be ascertained and the patient be kept in a comfortable and safe condition." I still say that hyoscine can be safely administered until its full physiological effects are manifested; but there is a vast difference between the physiological or remedial effects of a drug and its toxic effects. The toxic effects of hyoscine are extremely dangerous. On account of the great difference in the susceptibility of different persons for this drug no fixed dosage can be stated in advance, and only by the physician remaining with the patient and watching the effects of each dose, at least until his tolerance or intolerance has been ascertained, can this drug be used with safety. This precaution should be exercised in every case, because some persons are so susceptible to hyoscine that it is a very delicate matter to develop its physiological effects on them without going beyond that point and getting its dangerous toxic effects. It cannot be administered in a routine manner with safety.

Another peculiarity of this drug, or of persons taking it, is that in some cases prolonged administration begets intolerance instead of tolerance. This is rare, but in several instances I have found that after the patient had been under the influence of hyoscine for two or three days, and after all the visible manifestations of the drug, except dilatation of the pupil had subsided, a very small dose, one-fourth to one-half the size of those given in the earlier part of the administration, was sufficient to fully reestablish the effects of the drug, and that the delirium induced by such a dose was much more violent and prolonged than at the beginning. In such cases the prolonged administration would be dangerous.

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## POLYHYDRAMNIOS: ITS DIFFERENTIAL DIAGNOSIS AND TREATMENT, WITH THE REPORT OF CASES.

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*Case I.*—A multipara, much depressed in general health, with rapidly increasing distention of the abdomen, the cervix tightly closed, dilated by an elastic bag, the membranes ruptured artificially and compression made by a broad bandage held across the abdomen by assistants. Eleven quarts of amnotic fluid escaped. The fetus presented in a transverse position, and was delivered by podalic version. The placenta was removed, the uterus douched with antiseptic solution and tamponed. Abdominal compression was continued, the mother making a good recovery. The fetus had but little tissue in cord and brain; both were rudimentary in character. It was otherwise well-developed and was stillborn.

*Case II.*—A multipara, sent for removal of

cystic tumor supposed to be ovarian. During previous pregnancies had been well; during present pregnancy had much nausea and rapidly increasing distention of the abdomen, beginning at the fifth month. Urine practically normal; blood showed slight anemia. On examination, abdomen greatly distended; no fetal parts nor heart-sounds could be found. Finger passed through the cervix detected small fetal head floating in fluid. Diagnosis of polyhydramnios was made, membranes were ruptured, and about two gallons of fluid allowed to escape. Labor followed with twins, one of which had normal chorion and amnion with sac unbroken, the other had polyhydramnios. The placenta was large and edematous, the veins of the cord of one twin greatly enlarged and tortuous, and the tissue of the placenta and cord granular, with areas of cystic degeneration. The mother recovered well.

*Case III.*—Primipara, previously well. During early pregnancy excessively frightened by lightning. Was at the end of ninth month. Came into tedious labor with excessive amniotic liquid. Male child, weighing five and a half pounds, delivered by forceps. It breathed feebly and lived 10 minutes. Posterior portion of vertebral column and lower cervical and upper dorsal region deficient in development; meningocele present. Placenta thicker and larger than normal; quantity of amniotic liquid not much in excess; the cord very long and spiral. The mother made a good recovery.

*Case IV.*—Primipara, white, aged eighteen years. Mother died in confinement, cause not stated. Pelvis narrowed at the lower portion, expanded at the brim symmetrically; urine normal; patient fairly well nourished, and suffered little during pregnancy. Complained of pain in the right upper portion of the abdomen, dyspnea and sleeplessness. On examination, abdominal distention marked; fetus could not be outlined, nor could fetal heart-sounds be distinctly heard. The patient's lower limbs were considerably swollen, her heart-action labored. She complained of indefinite pains for several days, when the os was found fully dilated. The patient was given tincture of nux vomica; the membranes were ruptured, and compression applied to the abdomen. When the membranes ruptured, the head immediately engaged, the child descended and was allowed to emerge from the body of the mother gradually.

The placenta was removed, the uterus douched and packed with gauze. The mother made an uninterrupted recovery. The fetus gasped but did not breathe; its heart-beat persisted for three-quarters of an hour in spite of respiratory failure. Upon autopsy, general dropsy was found, and in the abdomen and pericardium a large quantity of fluid. The lungs were edematous; the kidneys showed atrophy of the pyramids, and the liver was softened and enlarged. The cord was shorter than the average, the placenta boggy, light in color, large and friable. The decidua was roughened, like a fibrinous exudate.

*Case V.*—Multipara, with moderate quantity of fluid. Dilatation well advanced, but pains inefficient because of overdistention of the uterus. Made patient sit upon a bucket; punctured membranes, and allowed several quarts of fluid to escape. Gave quinine and ergot. The child was speedily delivered, but failed to nourish properly, and died in 10 days with symptoms of intestinal obstruction.

By polyhydramnios is meant more than two pints of amniotic liquid at full term. As much as seven gallons has been seen in the human species. Pathology of the condition not fully known. Many conditions accompany polyhydramnios. The placenta often large, dropsical and infiltrated; Jungbluth's vessels often enlarged; amnion and chorion may be thickened, with extensive fissures in the epithelial layer of the amnion and fatty degeneration of cells. By experiment, seven times more fluid passes through veins than through arteries of cord into the placenta. Any fetal condition causing venous engorgement tends to produce polyhydramnios. Irritating substances formed in lymphatics may cause this condition. It does not result from increased renal action in the fetal kidneys. Excessive secretion from the cerebrospinal canal of the fetus may contribute to polyhydramnios. This condition is normal at the fourth month, and its persistence results from failure in normal development. By cryoscopy further information regarding the osmotic properties of maternal and fetal blood and of the liquor amnii may increase our knowledge. Bacteriology gives no information upon the subject.

The diagnosis is made by first diagnosticating pregnancy, then by observing that in polyhydramnios we can usually obtain evidence of faint uterine contraction, and can often insert the finger through the cervix and detect a presenting part. Ectopic gestation must be kept in mind, as polyhydramnios may complicate ectopic pregnancy. In ovarian cyst the illness is longer, the swelling at first unilateral. The intermittent hardening of the tumor is absent, and the uterus can be found but little enlarged. In ascites the dulness changes when the position of the patient is altered.

When pregnancy is found a second diagnosis must be made to recognize or eliminate the presence of pregnancy and ovarian cyst, pregnancy and ascites, plural pregnancy, hydatid mole, a very large child, or a malformed fetus. In hydatid mole the pear-shaped uterus has little fluctuation, and there is repeated discharge of blood. In large or malformed fetus the heart can usually be heard, and palpation reveals the child. While twin-pregnancy can generally be recognized, it may be completely mistaken for polyhydramnios. In exceptional cases ovarian cyst complicating pregnancy may be difficult to diagnosticate, and exploratory incision may be necessary.

Attention is called to misleading phenomena—the absence of such tension upon the membranes

as would be expected from the quantity of amniotic liquid, and also the absence of early shortening of the cervix.

Treatment by drugs is without value. When polyhydramnios is slight and not increasing, the patient's health remaining good, pregnancy should not be interrupted. When distention increases rapidly and the patient's health is impaired, under thorough antiseptic precautions the cervix should be dilated sufficiently to admit the finger. A pair of uterine dressing-forceps, closed, should be inserted, the membranes ruptured, the forceps opened, and a rent made sufficiently large to permit the introduction of the finger. Fluid should be allowed to escape very gradually until the presenting part descends firmly against the cervix. Firm pressure must be made over the abdomen by a many-tailed abdominal binder or broad bandage held by assistants. The patient must be watched, as labor is often precipitate and the fetus may assume unfavorable positions. Labor should not be hurried in the interests of the child, because the fetus is often deformed.

Polyhydramnios is dangerous to the mother from overdistention, relaxation, hemorrhage and increased danger of sepsis. The uterus must be completely emptied and made to contract. A hot intra-uterine douche of 1 per cent. lysol, tamponing with iodoform gauze, the hypodermatic use of strychnine and ergot and other stimulation are necessary.

Occasionally after abdominal section the excess of amniotic liquid has disappeared by absorption.

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## RECENT DISCOVERIES IN THE DOMAIN OF ETIOLOGY.*

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FOR a number of years past we have been accustomed to look to the science of bacteriology for advances in our knowledge of the etiology of disease. Since many of the specific diseases have been traced to bacterial origin we are constantly expecting new discoveries in this field, as there still remains a number of the more common specific diseases the etiology of which is undetermined. During the last few years there have been but few additions to our list of specific bacteria, notwithstanding the constantly increasing activity of bacteriologists. The lack of definite knowledge with regard to the etiology of yellow fever, typhus fever, syphilis, variola, varicella, rubeola, and possibly of scarlatina, as well as of certain other diseases, is not due to any want of attention on the part of bacteriologists, for current literature teems with reports of investigations in these particular fields. The results obtained in the study of some of these diseases are practically negative in character, in that they indicate that the bacteria encountered are either normal inhabitants of the body or merely accidental invaders that have no direct relation to the disease.

Recent studies upon yellow fever and variola in particular indicate that the explanation of this lack of progress in our knowledge of the etiology of disease is attributable to the fact that some, if not all, of the diseases enumerated are due to animal parasites, and that therefore the methods of the bacteriologist are inadequate for the discovery and study of the etiological factors of these diseases. The investigations that have been made indicate that the technic of parasitology is far more difficult than that of bacteriology in its present advanced stage of development. Perhaps one of the chief difficulties lies in the fact that so many of the investigators have not been trained zoologists, although a detailed knowledge if invertebrate zoology, especially of the Protozoa, appears essential to success in this line of research.

With the evolution of our knowledge of the etiology of malarial fevers, following the marvelous discovery and demonstration of Laveran in 1881, the possibility has suggested itself to many minds that at least some of the diseases, the etiology of which is as yet undetermined, may likewise be due to animal parasites. The investigations of Dr. Carlos Finlay of Havana, and those of Major Reed and his colleagues, upon the etiology of yellow fever are practically conclusive in demonstrating that yellow fever is due to an animal parasite which is transmitted in a manner somewhat similar to the transmission of malarial fevers, although the direct causative agent of the disease has not yet been discovered.

The bacteria encountered in cases of yellow fever may be classed as accidental invaders of the body, having no direct causative relation to the disease. The *Bacillus X*, discovered by Surgeon-General Sternberg in 1880, was found in only about 55 per cent. of the cases, and therefore could not be regarded as the etiologic factor in the disease. The *Bacillus icteroides*, discovered by Sanarelli, was found by that investigator to be present in less than 60 per cent. of cases and this fact at once led to doubt as to its direct causative relation to the disease.

The investigations of Major Reed and his colleagues show that yellow fever is not conveyed by formites, as was formerly held. These investigators were able to demonstrate that the disease is probably always conveyed by mosquitoes infected by sucking the blood of patients, and that these mosquitoes can convey the disease only when about twelve days have elapsed after they have become infected. This period of time is supposed to be necessary for the parasites to undergo a certain development in the body of the mosquito and pass from its digestive tract to the salivary glands.

Extensive bacteriological investigations upon the etiology of variola have demonstrated that the bacteria found in the lesions may be classed as

* Read before the Pennsylvania State Medical Society, September 17, 1902.

merely accidental invaders of the body having no direct causative relation to the disease. When examined before the fifth or sixth day the contents of the variola pustules are usually found to be sterile. The bacteria found in the older lesoins are staphylococci, streptococci and organisms belonging in the group of pseudodiphtheria bacilli. These bacteria are constantly found on the skin and mucous surfaces of healthy persons, and therefore can have no causative relation to the disease.

Van der Loeff, L. Pfeiffer, Guarneiri, Doehle, E. Pfeiffer, Wasielewski, Reed, Funck, Gorini, Ishigami and others have described peculiar glistening bodies in the contents of variola pustules, and in the blood of variola patients, which they regard as parasites. Van der Loeff, in 1886, was the first to regard these bodies as the etiological factors of the disease, and classed them with the *Rhizopoda*. In 1887 L. Pfeiffer made an independent discovery of the parasite which he called *Monocystis epithelialis* and classified it among the *Acystosporidia* of Labbé. In 1892 Guarnieri reported on his method of cultivating the parasite of vaccinia in the cornea of rabbits. He considered the organism of vaccinia as a modified form of the parasite of variola, and proposed the name *Cytoryctes variolæ, vel vaccinæ*. The names given to the parasite by L. Pfeiffer and Guarnieri give prominence to its peculiar affinity for epithelial structures. Ogata regarded it as a polycystic *Gregarine*. Funck gave it the name *Sporidium variolæ*. Ishigami also classes it among the *Sporozoa* and regards it as similar to *Microsporidium bombycis*, though he does not attempt to classify it definitely.

My own investigations upon variola and vaccinia have led me to the opinion that variola is caused by an animal parasite belonging in the class *Sporozoa*, and that vaccinia is due to a modified form of the same parasite. This opinion seems self-evident from the mere fact that vaccinia protects against variola. There are, however, other reasons for this opinion, as, for instance, the fact that it has been demonstrated that by passing the parasite of variola through several monkeys it can be transferred to heifers and finally to human beings, and then it gives rise to typical vaccine vesicles. The nature of the modification which the parasite undergoes in its passage through bovines has not yet been demonstrated. It may be merely an attenuation in virulence which persists through many generations, probably indefinitely, or it may be some modification in the mode of development, though no such modification has been discovered.

Considerable criticism has been made of the opinion that the peculiar bodies found in variola and vaccinia are animal parasites. The opinion of those who oppose the parasitic theory is that the bodies seen are merely degenerated nuclei of leucocytes and epithelial cells. It seems to me that the strongest arguments in favor of the parasitic nature of these bodies are the facts that they present ameboid movements at certain stages of their development, and that they form sporocysts as seen in the older lesions and in crusts, as well as in variolous material cultivated in collodion capsules placed in the peritoneal cavity of rabbits. These facts give very strong presumptive, if not positive, evidence that the parasite presents two modes of development—asexual and sexual—similar to the modes of development of other well-known *Sporozoa*.

The parasite of variola is probably transmitted through the air or by direct contact, as is the case with many bacterial diseases. There is no evidence that insects play any part in disseminating the disease, except that flies may carry the infectious agent on their bodies from association with cases of variola, and thus assist in its dissemination. In the same manner money and other articles may become the carriers of the organisms. From the fact that the parasite of variola has an especial affinity for epithelial structures it is probable that infection takes place by way of the mucous surfaces of the nose and throat.

One of the most interesting and important discoveries in recent years in the domain of etiology is that pertaining to the etiology of the so-called "spotted fever" of the Rocky Mountains by Drs. Wilson and Chowning (*Jour. Am. Med. Assoc.*, July 19, 1902). This disease is peculiar to circumscribed areas of Montana and Idaho, along the eastern foothills of the Bitter Root and the southern foothills of the Boise mountains.

Bacteriological examination of the blood and tissues of persons dying of the disease revealed only well-known species of bacteria normally present in the body. On the other hand, the blood was found to contain large numbers of a parasite somewhat resembling that found in Texas fever of cattle, although it is larger than that organism and possesses ameboid motion. The organism varies greatly in form, size and staining reaction at various stages of its development. The smallest forms are one to two microns in size, ovoidal in form, and possess no ameboid movement. Another phase of the parasite is usually ovoidal in form, from three to five microns in size, and possesses ameboid movement. In freshly drawn blood bodies are sometimes found that resemble diplococci which are 0.5 to one micron in size and are without movement. These forms are extracellular, and stain faintly with methylene blue.

The organism of "spotted fever" is a *hematozoon*, and is found in the red blood-cells in the circulating blood, but more plentifully in the blood-cells lying in the congested capillaries of the tissues. The fact that no pigment was found in the organism leads the discoverers to conclude that the parasite belongs in the class with the Texas fever organism, and not with the malarial group.

Wilson and Chowning believe that the parasite is conveyed to man by the bite of ticks, several species of which are found in the infected locality. Though no infected ticks have yet been

encountered, there is strong presumptive evidence that they serve as the carriers of the parasite, from the fact that the disease prevails at the season of the year when the ticks are prevalent, that is, from March to July.

Inoculation experiments upon rabbits with the blood of a fatal case were successful, the parasites persisting in the blood of the rabbit for four weeks.

The discoveries made thus far lead us to hope that the etiology of the remaining specific diseases may be ascertained by research along similar lines. The nature and mode of dissemination of the exanthemata is in many respects similar to variola, and should lead to investigations from the view-point of animal parasitology. If these diseases are due to animal parasites, the problem of discovering and studying the etiological factors is a difficult one because of the minute size of the organisms.

## MEDICAL PROGRESS.

### HYGIENE.

**Disinfection for Yellow Fever.**—The theory that a certain mosquito, the stegomyia, is the sole means of transferring, or, more properly, infecting yellow fever is a recent product of medical science, and was hardly enunciated before it was conclusively proved. W. C. GORGAS (Lancet, September 6, 1902) summarizes the results in Havana during the year 1901 of disinfection for yellow fever under the hypothesis that the stegomyia mosquito is the only means of transferring the disease. Prior to making a crusade against the mosquito itself, the usual methods of quarantine and disinfection were carried out in the houses of the sick, in the most perfect way that knowledge and care and money could produce, as this work was carried on by the United States Government. Yet these plans, rigorously prosecuted, were insufficient, and the disease spread in spite of them. When the question of the mosquito and his destruction came up, the following points had to be covered: (1) To destroy all the stegomyia they could, so as to limit the number of insects capable of conveying disease; (2) to prevent the stegomyia they did not destroy from biting yellow-fever patients, for if that could be accomplished, disease could also be prevented; (3) to destroy all mosquitoes which might have or actually had bitten yellow-fever patients, and thus become infected, because if these were killed it is obvious that disease would be limited. With the object in view of reducing the number of mosquitoes, orders were issued, commanding all people within the city limits to keep receptacles containing water mosquito-proof. Similarly all bodies and stagnant collections of water were treated with oil, and every possible means taken to destroy the insect. To meet the second proposition—keeping the mosquitoes and the infected patient apart—all hospitals and dwellings with yellow-fever patients within them were thoroughly screened, and inspectors put on guard to see that the screens were not left open. To meet the third proposition—to kill infected mosquitoes within the hospitals and houses—at the time the work was begun pyrethrum powder, 150 pounds on the average for each case, was used, and in addition to it those methods of disinfection which had been carried out previous to the crusade against the insect. Mere figures in all statistics lie, notwithstanding the old adage to the contrary, because mere numerals give no adequate idea whatever of the surroundings and factors of the case, which never can be disregarded. So far as statistics are valuable, however, the results of this treatment in Havana for 1901 show 18 deaths from yellow fever, which is the lowest the city records show since 1856, prior to which no records whatever of such subjects are extant. The special significance of this remarkably low total is that the floating population of Havana, mainly of non-immunes, was no less, if it was not even greater, during 1901 than for the preceding ten years. The factors, therefore, which make Havana peculiarly the victim of yellow fever were not removed, while beyond all human doubt the causes of transferring the disease were very largely corrected.

### MEDICINE.

**Bronchopneumonia in Children.**—Of the diseases which attack the lungs of infants bronchopneumonia is the most common and serious. The treatment of this disease is discussed by JOHN L. STEVENS (Lancet, September 20, 1902), as follows: Not the least important point in the treatment is the prophylaxis. It is to be remembered that every common cold or bronchial catarrh or gastro-intestinal disorder in a young infant may pass into this exceedingly serious and fatal disease. It is obvious then that everything should be done to prevent such an occurrence. No indisposition of the kind indicated in an infant should be regarded lightly, and the child should be carefully treated and not lost sight of till all symptoms of these initial disorders have passed away. In particular the mother snould be warned of the danger of exposing the child to cold, and of the necessity of keeping it warmly but not heavily or tightly clad; and gastro-intestinal derangements should be carefully corrected by directions as to diet. In the presence of the acute disorder itself the most important point to bear in mind is the fact that we are dealing with an acute, generalized, inflammatory disease of the respiratory apparatus, the immediate tendency of which is to produce great exhaustion of the vital powers. The disease is essentially one of debility, and treatment should aim at maintaining nutrition and stimulating the failing heart. All measures tending to depress the child should be strictly avoided, and for this reason emetics are not to be used. Place the child in an airy, well-warmed room. If it can be easily arranged, let the air near his bed be moistened by the steam from a bronchitis-kettle. This will often have a marked effect in soothing the cough. Do not load the child with clothes, but keep him warm, and avoid compression of the chest and abdomen by flannel binders. Two or three linseed poultices in the course of the 24 hours, applied back and front, and not too hot, are often of service as mild counter-irritants. Feed the child with milk diluted or peptonized, and check diarrhea with subnitrate of bismuth, combined if necessary with one or two grains of Dover's powder. Alcoholic stimulants are almost always necessary, but they should be strictly supervised by the medical practitioner, ordered by him as occasion demands, and prescribed as Sturges recommends—in minims, not in drams. A mixture containing from half a grain to a grain of carbonate of ammonia and two minims of tincture of digitalis in each dose, made up with sirup, may be given every three or four hours. The child should be constantly watched by a competent nurse, and should be occasionally held up to relieve breathing.

**Diagnosis of Hour-Glass Stomach.**—The condition of hour-glass stomach, as it follows carcinoma, perigastric adhesions, or ulcer is undoubtedly very difficult of diagnosis. The most prominent symptom, according to J. DECKER (Münch. med. Woch., September 16, 1902) is an exceedingly severe gastric pain, differing

from that of an ulcer in that it is of much longer duration and more a feeling of tension than a cramp. It may persist for half an hour after the vomiting, and is relieved after some time with rest and fluid diet, though it returns at once when the patients get up and take more solid food. The vomiting is generally in small portions, and varies in time of appearance with the seat of stricture; if in the middle of the stomach, generally within two to three hours. If by these signs the condition is suspected, it can be rendered more positive by washing out the stomach, for the water will return clear at first, and then suddenly with particles of food. It may also be impossible to remove the first portions of water, since these disappear in the more distal portion of the sac. On inflating the stomach with air, the constriction may be evident, and the esophageal portion swells up first. Gastrodiaphany may also aid, in that it permits a shadow to appear at the stenosis. Finally pressure on the inflated stomach may give rise to a sound due to the rush of air from one half of the stomach to the other. The patients are generally exceedingly nervous owing to their chronic state of suffering, and their condition is frequently treated as nervous dyspepsia before recognized.

**Early Diagnosis of Typhoid.**—The blood has been systematically examined by H. Schottmuller (Münch. med. Woch., September 23, 1902) for typhoid bacilli, and positive findings have been obtained in 84 per cent. The technic is very simple. A rubber bandage is rolled around the arm, and then about 20 c.c. removed from the veins at the elbow with a sterilized Luer syringe after the parts have been carefully cleansed with ether. The blood is then passed into several tubes of liquefied agar kept at 45° C., so that to every six cubic cm. of the medium there are two to three of blood. After shaking, the mixture is then plated and kept at 37° C. The typhoid colonies can be recognized by their dark greenish-black color in the depths and dark grayish hue on the surface. If on examinaton they are found to contain motile bacilli, the diagnosis is positive without further examination, since no other germs of this character were ever found. In children the results were less frequently positive, which is in accordance with the milder course generally observed. It is of great significance for the early diagnosis that the bacilli were obtained from cases that presented themselves for treatment as early as from the second to the fifth day of the disease, and also during the first 24 hours of a relapse after an afebrile interval of two to three weeks. Success was less frequent during the amphibolic stage, and in those cases where the temperature-curve was chiefly remittent or intermittent. An interesting observation is the fact that the blood was frequently found to contain bacteria in the ephemeral rises of temperature up to 104° F. and higher. A proof of the presence in the blood of antityphoidal bodies is to be found in the much slower development of the colonies if the blood is taken late in the disease. The shortest time in which colonies can be identified after plating is 20 hours; generally, however, it takes two or three days. From a prognostic view it may be said that few colonies during the acme suggest a mild course, and vice versa. It is proper to regard each case of typhoid as a specific form of bacteremia, and it is probable that the bacilli reach the blood through the inflamed mesenteric glands. It is even possible that the ulcers in the intestines are the result of metastatic infection.

**Glycosuria and Tabes.**—The relation between glycosuria and tabes is a close one, since in diabetes secondary nervous disturbances may occur, localizing themselves in the posterior columns, and since in tabes there may be changes in the fourth ventricle leading to an excretion of glucose. That it may be difficult at times to decide which is the primary condition is clear from the case related by E. Meyer (Münch. med. Woch., September 16, 1902), where a positive Romberg, sluggish pupils and some sensory disturbances were present, and where the urine contained from three to five per cent. sugar. Since, however, an antidiabetic diet improved the condition but little, and since the administration of pure glucose was not followed by any increased excretion, it was decided that the tabes was primary and was accompanied by an affection of the nuclei at the floor of the fourth ventricle, which control sugar metabolism.

**Anemia Due to Small Hemorrhages.**—In certain instances the daily loss of even small amounts of blood may produce very severe anemias. J. B. Herrick (Jour. Am. Med. Assoc., September 27, 1902) has found that bleeding hemorrhoids may often cause this condition, and that recovery is almost certain after the proper remedial measures have been undertaken. He reports five cases which exemplified this condition, the anemia being of the pernicious variety, and recommends that when a blood examination shows a chlorotic or secondary type immediate operative measures for checking the hemorrhage should be instituted.

**Alimentary Glycosuria and Levulosuria in Hepatic Diseases.**—After a careful review of the literature bearing upon alimentary glycosuria, L. Ferrannini (Rif. Med., September 6, 1902) calls attention to the fact, established by Minkowski, that after ablation of the pancreas the liver no longer has the power to convert glucose into glycogen, while the transformation of levulose is accomplished without difficulty. Levulose, thus transformed, is stored up in the liver and reaches the circulation only in small quantities. Glucose, on the other hand, remains unchanged, the greater part passing into the circulation and thence to the urine. Minkowski found in the livers of dogs affected with pancreatic diabetes but a small trace of glycogen after administration of glucose, while ingestion of levulose by dogs so affected caused the appearance in the liver of glycogen in considerable quantities. Ferrannini therefore holds that in hepatic diseases induction of alimentary glycosuria with levulose is of greater diagnostic import than the production of that condition with glucose. The comparative results of administration of both substances by the author in 16 cases affected with various abnormalities of the liver seem to indicate that levulosuria is indeed a more reliable index of insufficience of the glycogenetic function of that organ than glycosuria.

## PEDIATRICS.

**Split Proteid in Infant-Feeding.**—So little is known either here or abroad of the physiologic difference between the proteids of cow's and of human milk that it is a great advance to be able to approximate the proportion of whey proteid to caseinogen in preparing artificial foods. Dr. Thomas M. Rotch of Harvard, in an address before the British Medical Association (Br. Med. Jour., September 6, 1902), said that this use of the split proteids, which had been introduced largely through the experiments of Drs. White and Ladd, was probably the most important step in advance which had been taken in recent times. Their conclusions were as follows: (1) By the use of whey as a diluent of creams of various strengths cow's milk can be modified so that its proportions of caseinogen and whey proteids closely correspond to those in human milk; (2) the whey must not be heated above 69.3° C. or its proteids coagulate: 65.5° C. destroys the rennin enzyme; (3) the emulsions of fat in whey, barley-water, gravity cream and centrifugal cream mixtures were the same, and though the

combination of heat and transportation may destroy the emulsion in any modified milk, this may surely be prevented by keeping the milk cool during delivery; (4) whey-cream mixtures yield a much finer, less bulky and more digestible coagulum than plain modified mixtures with the same total proteids. It is clear that the use of barley-water, which gives the next finer coagulum, is not indicated. The tenacity of the whey coagulum is not influenced by the proportion of fat present, and whey, while not so important in its mechanical action in affecting the coagulum as the cereal diluents, still had a pronounced power in that direction. In very young infants the total proteid should be about 0.75. Of this 0.50 should be whey albumin and 0.25 caseinogen. When the infant has reached an age where it requires a higher total proteid than 1.75, on account of our lack of chemical knowledge we must begin to give whole proteid.

**Pertussis and Scillitic Oxymel.**—About 57 observations have been collected by Boulade in the Children's Hospital of Paris, and made the topic of an inaugural essay by J. COMBY (Sem. méd., September 24, 1902), concerning the use of scillitic oxymel in the treatment of whooping-cough. This medicine is prescribed in its pure condition, as originally suggested by Netter of Nancy in 1886, in a dose of two after-dinner coffee spoonfuls for each year of the child's age, and is administered preferably between five and six o'clock in the afternoon. He reports that it has never failed to decrease the number and intensity of the attacks, and to give the child comparatively quiet nights. Unlike belladonna and atropine, its usefulness continues throughout the course of the disease, and appears to exercise a direct influence upon the evolution. Moreover, the medicine is ordinarily taken well by the little patients and has the advantage that it can be borne perfectly well by the average city patient.

**Hepatic Cirrhosis in Childhood.**—In commenting on the various forms of this disease found in infancy and childhood J. L. MORSE (Bost. Med. and Surg. Jour., September 11, 1902) advances the following explanation of cirrhosis found in connection with congenital obstruction of the bile-ducts: "Irritant substances may pass through the placenta to the fetus, going directly to the liver, or reaching it indirectly after passing through the general circulation. The cholangitis then descends to the larger ducts. Stenosis and obliteration readily follow, because of the extremely small size of their lumen at this time. The conditions for a mixed cirrhosis are thus produced." Additional points in favor of primary cirrhosis are: The constant occurrence of cirrhosis in obstruction of the bile-ducts in infants, compared with its rarity after obstruction of the larger ducts in adults; the large size of the liver, which is usually small when due to obstruction in later life, and the enlargement of the spleen, which does not occur in uncomplicated biliary obstruction.

**The Production of Ferrated Milk.**—It has been discovered as the result of numerous experiments on animals performed by L. GIORDANI (Rev. mens. Mal. l'Enf., September, 1902) that the subcutaneous administration of iron in increasing doses is followed by the appearance of this element in the animal's milk, in quantities from two to five or more times as great as when iron is administered per os. This drug appears in the milk in organic combination, in which form it is easily absorbed and assimilated by the infant. The modifications in the various constituents of the milk provoked by the injection of the citrate of iron are quite negligible. The quantity of milk is slightly diminished. An animal can tolerate large doses of the medicament provided these are attained gradually and with intervals of rest. No inconvenient local reaction is produced. The author concludes from his researches that one may hope to obtain a ferruginous milk of peculiar value in infantile therapy.

## BACTERIOLOGY.

**Tubercle Bacilli in Urine.**—In view of the uncertainty of finding the tubercle bacilli in specimens of urine naturally voided, the following method is advanced by J. P. BRYSON (Jour. Cut. and G.-U. Dis., September, 1902). He had observed accidentally that the urine drawn by catheter after voluntary micturition contained a relatively greater number of bacteria. He made a series of comparisons in well-marked cases of tubercular cystitis, pyelonephritis, etc., and in each case found numerical disproportion between the numbers of the bacilli in the tidal and residual urines, the greatest number being always seen in the urine drawn with the catheter.

**Germ of Smallpox.**—An interesting account of the work done to discover the cause of smallpox is given by W. DOMBROWSKI (Zeitsch. klin. Med., VOL. 46, Nos. 1 to 4). Certain authors have described bacteria, but the majority mention cocci similar to the staphylococcus as being contained in the pustules, none having recorded any successful animal experiments. Hopes of finding specific bacteria became less and less. On the other hand, the proof that chemical substances were not the inciters was soon forthcoming, and the mystery which overhung the whole subject was not cleared until certain investigators began to describe peculiar bodies, apparently belonging to the protozoa, as invariably present in the lesions. These observations the author can verify from his own studies. If, after previous sterilization of the skin, a vesicle be punctured and a drop of the clear fluid be examined with the oil-immersion, a large number of dark, rounded or more oblong bodies, surrounded by a lighter area, will be found to crowd the field. They are found to be actively motile, and two different excursions can be discerned, one pendular and rapidly executed, and another slower and progressive in character. On the second day, besides these bodies, others will be present from two to three times as large, transparent and with indistinct contours. In the center of these hyalin masses there are four dark granules which constantly change their position. During this period leucocytes are already present, chiefly of the polynuclear variety, and their number increases more rapidly in the milder cases. By the time the exudate has assumed the characters of pus, fewer of the above described bodies are found, but instead there are larger, regularly formed spheres of yellowish color and white areola, situated within the protoplasm of the leucocytes, or free, with or without motion. Very often diplococci are also present or bodies possessing the general shape of yeast. Reproduction probably goes on solely by budding. The organisms of the abscesses do not differ in any way from those of the pustules, except that the spheres are more prominent. Anilin dyes, such as Löffler's or Ehrlich's solutions, do not stain the bodies, and a number of empty spaces are seen in their place, but retaining the general contours. In fresh blood-preparations the smaller structures of the pustules can invariably be seen either free or within the red or white blood-cells. By inoculating culture media with the contents of variola pustules no known variety of bacteria can be grown, so that there is no question that the suppuration is due to the specific organisms and not to secondary infection. These specific bodies, while they do not grow, retain their vitality for months on agar, the free bodies becoming less and the medium-sized yellow spherules increasing in number. Blood smeared on agar loses its red color, and the surface becomes white, broader and thinner, and contains the

same structures. It is most likely that they are all different phases in the development of the same parasite, whose exact nature is not clear, but which is probably best classified among the blastomyces. Animal experiments were not made by the author.

## PATHOLOGY.

**The Influence of the Extirpation of One Kidney On the Organism.**—In an experimental work Ssokoleff (Bolnit. Gaz. Bot., Nos. 18, 19 and 20, 1902) studied the influence of the extirpation of one kidney on the muscles, blood-vessels and nerve-centers of the heart; also on the other kidney and the liver. The influence, according to his findings, of such a nephrectomy is identical with the influence of a ligature of one ureter or one renal artery. In all these conditions there takes place a hypertrophy of the heart, preceded by a parenchymatous nephritis, which in its further development changes into a glomerulonephritis. As a result of his work the author also comes to the conclusion that the hypertrophy of the heart accompanying chronic Bright's disease is not due to any mechanical influence, but is most probably a result of some secondary chemical influence.

**On the Etiology of Noma.**—As the bacteriological examination of the patients of Dr. Korsch (Bolnit. Gaz. Bot., No. 24, 1902) showed the presence, among others, of the diphtheria bacilli, he added to the usual course of treatment an injection of diphtheria antitoxin, after which the defect began to cover itself with healthy granulations, and the patient's general condition to improve. Though the diphtheria bacillus may be only a secondary factor in the etiology of noma, still the author thinks that it is certainly not an indifferent agent, and consequently, whenever it is found, antitoxin should be added to the rest of the treatment.

**Change of the Hemolytic Power of Blood-Serum.**—Glinchikoff (Bolnit. Gaz. Bot., No. 30 and 31, 1902) in the examination of the strength of the hemolytis of dogs' blood-serum against rabbits' erythrocites, found that the process of digestion increases the hemolytic power of the serum, and that the increase reaches its maximum seven hours after the meal. Further he found that, of the different foods, fat increases the hemolytic power most, meat does it least, and bread and milk occupy in regards to the hemolytic power a position between fat and meat.

**Diphtheria, Tetanus Toxin and Hemoglobin.**—Dr. Kukharshevsky (Russky Vratch, No. 29, 1902) found that after a subcutaneous injection of diphtheria toxin in a rabbit the number of the erythrocytes becomes diminished, while the number of the white corpuscles is increased. The specific gravity is increased, and the quantity of hemoglobin diminished. The result of injection of tetanus toxin is the same, with the exception of the specific gravity, which after the injection of tetanus toxin becomes diminished.

**New Blood Reagent.**—The old method of examining spots, etc., for blood by means of sodium chloride and glacial acetic acid has been modified by C. Strzyzowski (Ther. Monatsch., September, 1902), who uses the following formula: Glacial acetic acid, water and alcohol, each one c.c.; hydriodic acid, three to five drops. This mixture does not keep well and should be mixed ready for use. The substance to be examined is placed on a slide, a sufficient amount of reagent added to cover it, and the mixture then boiled for 10 seconds. The crystals thus obtained are larger and more perfect than by any other method. If the suspicious substance is fluid, it is best to evaporate it to dryness on a slide.

**Fibroma of the Ovary.**—From a study of the recorded cases of this condition, it is possible to recognize three ways in which a new growth of a fibromatous or fibromyomatous character may involve the ovary, says John S. Fairbairn (Jour. Obstet. and Gyn. Brit. Emp., August, 1902). (1) The whole ovary may be converted into a hard tumor, maintaining to some degree its original shape, but bearing no recognizable portion of the original structure. This is an unusual occurrence. Attention may be directed to the fact that this complete fibrous transformation does not depend upon the size to which the tumor has attained. It takes place in small as well as large tumors, and does not depend upon the growths having reached a size sufficient to destroy the ovary. It is difficult to understand why the pathologic change should affect the whole stroma from the first, as this is more like an inflammatory fibrotic change than a new growth. (2) The growth forms a hard tumor within the ovary, which it spreads over its outer surface, so that it remains more or less encapsulated within the organ. The amount of ovarian tissue remaining appears to depend rather upon the position of the growth in the ovary than on the size the growth has attained. With the increase in size of the tumor the capsule tends to become more thinned out and less separable, so that the encapsulation may be recognizable only near the attachment of the ovary. Virchow has stated that the growth often originates in the outer end of the ovary. (3) The new growth forms a pedunculated tumor attached by a pedicle to the ovary. Some of these growths may be from the ovarian ligament. Keiffer suggests that fibroma of the ovary may follow part of their development in the center of the gland, and then be extended towards the periphery, and become pedunculated like subperitoneal fibroids of the uterus. The age limit is a wide one, varying between twenty-seven and sixty-seven. The general health is not usually affected. Trouble with micturition may occur due to pressure upon the bladder, if the tumor be large. The same condition may cause pain. The menstrual function may be interfered with by prolongation of the period or increase in the flow. This is not the rule.

**Researches on Cancer.**—As the result of investigations extending over a period of several years, E. v. Leyden and F. Blumenthal have published a preliminary communication (Deut. med. Woch., September 4, 1902). The transmission of carcinoma from man to the lower animals was unsuccessful, both rats and mice being fed with the infected tissue for months without any results. They did, however, succeed in transmitting cancer from one dog to another. Curative attempts in dogs were also made by injecting the serum of rabbits which had been subjected to subcutaneous injections of liquefied cancer-tissue for several weeks. A very favorable result was secured in all cases, the tumor undergoing a liquefaction and a reduction in size. A freshly extirpated carcinoma from a dog was used, by means of crushing and extraction, to prepare a serum which, when injected into another carcinomatous dog, produced the same favorable effect. In like manner trials were made in human subjects, all inoperable cases. No bad after-effects were noted. In two cases which ended in death, having been far advanced in the disease, no change was noted in the tumor itself, but at autopsy no metastatic growths were found, and neighboring lymph-nodes, which had been palpable and probably infiltrated, had disappeared. In a third case, accompanied by extreme pain and cachexia, a marked improvement in the general condition was noted, although no favorable change could be seen in the tumor.

**Formation of Toxoids in Tetanus Cultures.**—Through recent experiments, A. Bonome (Rif. Med., August 30, 1902) discovered that the soluble products of the bacterium coli, that is to say, the coli toxins, possessed the power to retard the development of the tetanus bacillus when mixed with the culture medium

for the bacillus in the proportion of one-fourth of the former's volume; and further, that the quantity and activity of tetanus toxin developed in such a medium was lessened. This diminution was not due to attentuation of the bacilli, as proven by the toxic effect of their inoculation into animals after having been for some time subjected to the influence of such a culture-medium; but rather, in the author's opinion, to a modification of the tetanus toxin by the nutrient medium through which the toxic element was in great part destroyed. Experiments upon guinea-pigs showed, however, that that part of the toxin which excites "immunizing reaction" in living protoplasm was unchanged by the influence of the coli toxin; for injections of the filtrates of cultures which had been subjected to its action, as before described, failed to induce tetanic symptoms, and produced a certain degree of immunity to injections with virulent tetanus cultures. This immunity is believed by the author to be due to the deelopmevnt of tetanus toxoids derived from the splitting up of the tetanus toxin in the presence of the bacterium coli, the toxoid possessing the power to excite formation of tetanus antitoxin in the body of the living animal. It is hoped that the knowledge of the production of tetanus toxoids in this manner may find a practical application in the immunization of animals, especially those in general use for the production of antitetanic serum, and which, from their great susceptibility to the tetanus toxin, frequently succumb during the period of immunization.

**Tetanus and Vaccination.**—During the year 1901 an unusual number of cases of smallpox developed in the United States, and in that period a much greater number of people were vaccinated than in any previous year. Joseph McFarland of Philadelphia (Lancet, September 13, 1902), after a prolonged study of cases from all over the world, reports that the infections have been confined almost exclusively to the United States east of the Mississippi and to eastern Canada. (1) Tetanus is not a frequent complication of vaccination; (2) the number of cases observed during 1901 was out of all proportion to what had been seen before; (3) the cases have nothing whatever to do with atmospheric or telluric conditions; (4) a small number occurred after the use of various viruses; (5) an overwhelming number occurred after the use of a certain virus; (6) the tetanus organism is in the virus in small numbers, being derived from the manure and hay; (7) occasionally through great carelessness or accident the number of bacilli becomes greater than usual and may lead to the epidemic occurrence of tetanus; (8) the cure for the danger lies in greater care during the preparation of the virus.

## SURGERY.

**The Iliopsoas Bursa.**—Attention is called to the surgical importance of this bursa and to the treatment of its inflammatory conditions by F. B. LUND (Bost. Med. and Surg. Jour., September 25, 1902). This bursa lies beneath the musculotendinous portion of the iliopsoas muscle and in front of the capsule of the hip-joint. Its position and frequent connection with the hip-joint may cause its involvement in osteo-arthritis, gonorrheal infection, or suppurative arthritis of the joint, and the symptoms due to the disease of the bursa may dominate the clinical picture. The writer has made a series of dissections to determine the size and position of the bursa, and in 18 subjects found a free communication with the hip-joint in three cases, and an extension over the pelvic brim in nine cases. He also reports three cases of suppuration in this bursa which came to operation. In gonorrheal cases incision of the bursa affords an easy method for reaching and draining the joint, and in osteo-arthritis relief of pain is afforded by incision of the bursa. The author finds that the best incision is one just below Poupart's ligament between the anterior crural nerve and the femoral artery. Iliopsoas bursitis should be more often considered in the differential diagnosis of obscure tumors in the groin, especially in cases where the hip-joint is known to be diseased and where a tumor suddenly appears in front of the joint, which is painful and tender, and affords a sensation of deep fluctuation.

**Operative Treatment of Varicose Veins.**—Since some doubt still exists as the value of the various operative measures employed in the treatment of varix, J. B. BLAKE (Bost. Med. and Surg. Jour., September 25, 1902) thinks that it is desirable in the future to settle the following points: (1) To determine how often the deep veins are actually and clinically affected, in connection with superficial varicosities, and how it is possible to determine the condition of these deep veins before operation; (2) to subject a large number of cases of all degrees of varicosity and its complications to the same method of treatment, and to trace the results carefully for one or two years.

**Value of Sublamin.**—Concerning sublamin, an organic derivative of mercury, recommended in the place of sublimate for hand-disinfection, M. BLUMBERG (Münch. med. Woch., September 16, 1902) says: (1) It equals in strength the best known disinfectant, sublimate. (2) It possesses the advantage over sublimate that it does not irritate the skin in high concentrations, and hence can be readily employed where the hands have come in contact with highly virulent matter. (3) There is a much greater tendency to penetrate and to act in the depths of the tissue. (4) Owing to rapid and easy solubility in water, strong solutions can easily and quickly be made, even if the salt is compressed into tablets.

## GENITO-URINARY AND SKIN.

**Electrolysis and Xanthelasma.**—Incision of xanthelasma is often accepted with difficulty by the patient through fear of scars which may be more disfiguring than the disease itself. It is therefore well to draw attention to the good effects recently obtained by L. LEPLAT of Liège and M. PAMSIER of Avignon (Sem. méd., September 24, 1902). These men have employed electrolysis at irregular intervals during perhaps the last 15 years, and at the present time are using it systematically. They insert a platinum needle, preferably attached to the negative pole, while the positive pole has an ordinary sponge electrode, held upon the cheek of the patient. Leplat uses currents between two and four milliampères in strength. Pamsier, however, does not hesitate to use stronger currents, from six to ten milliampères in extensive cases according to the degree of the disease. It is often necessary to puncture the tumor many times with the same needle, which is the usage of Leplat, or, according to Pamsier, many needles, attached to one electric pole, may be driven into the tumor at one sitting. It is advisable to pass the needles very obliquely through the skin. In order to check the pain caused by the passage of the current it is well to use cocaine. On the other hand, it must not be forgotten that these injections promote edema of the eyelid, and occasionally ecchymosis. Preceding the electrolysis it is well to rub the eyelid with an ointment consisting of three drams of menthol and three of hydrate of chloral in six of lanolin.

**Vesical Calculus.**—A unique case is reported by D. C. HUFFMAN and F. W. ROUSH (Jour. Am. Med. Assoc., September 27, 1902). The patient had been wounded during the Civil War, a ball entering the upper part of the thigh near the groin. The wound healed and the ball was never found. Forty years later vesical

symptoms appeared and a diagnosis of calculus was made. Suprapubic lithotomy was performed, and a calculus weighing 580 grains and encysted in a cul-de-sac near the neck of the bladder was removed. Its nucleus was a flattened lead musket-ball. This probably did not penetrate into the cavity of the bladder until the beginning of the appearance of the vesical symptoms, and got through the wall by the slow process of ulcerative absorption.

**Faradization and Pruriginous Dermatoses.**—The use of the faradic current as a means of calming pruritus has recently been recommended by Bouveyron of Lyons (Sem. méd., No. 25, 1902). He finds that its results are similar to those exercised by static electricity and that it has the advantage of not necessitating the installation of a complicated and costly apparatus. The small induction coil which is in common and habitual use in medical practice, and the electrodes which accompany it, are usually sufficient. This author has tried the effect of the faradic current in all kinds of itching skin diseases, such as eczema, lichen, pityriasis, rosacea, morphea, etc. His results have been practically the same in all. This treatment, however, has failed in two cases of senile pruritus. Not only does the current usually control the itching, but also exercises a curative effect upon the disease, and has not been known in his hands to give any harmful result. The positive pole appears to produce less calming effect than the negative.

**Simple Ulcer of the Bladder Combined with Round Ulcer of the Stomach**—Dr. Kavetsky (Prac. Vratch, No. 24, 1902) reports an autopsy with this rather rare finding: In May, 1899, the patient had a urethrorrhagia lasting for six weeks, for which the uterus was curetted. After a while she began to suffer again from urethrorrhagia, and in October she again entered the Hospital, had there an attack of relapsing fever, recovered from it, and in December was again curetted. On the evening of the operation the temperature rose to 102.4° F., and continued between 99° and 101.3° F. for 12 days, when the patient died. At the autopsy there was found in the peritoneal cavity some 500 c.c. of serous fluid, adhesions all around the different organs of the peritoneal cavity, and a simple round ulcer on the small curvature of the stomach. The bladder had adhered to the pelvic peritoneum, and on its posterior wall there was a perforated ulcer of 4 to 5 mm. in diameter. This opening led into a pus cavity, which lay between the uterus and the bladder. The author thinks that both ulcers are due to circulatory deficiency caused possibly by the relapsing fever. There was no indication in the clinical history of any trouble in the stomach or bladder.

## PHYSIOLOGY.

**Effect of Fatigue upon the Kidneys and Liver.**—The peculiar substances circulating in the fatigued body, according to G. Guerrini (Arch. Ital. Biol., vol. xxxvii, fasc. 11, 1902), induce certain well-defined cellular changes. The reaction of the cells of the kidneys and liver to such substances, as determined by recent experimental research conducted by the author, is given as follows: In the kidneys, the greatest changes were seen in the cells of the convoluted tubules and in the ascending limb of Henle's loop; the Malpighian corpuscles and the straight tubules being almost normal in appearance. The protoplasm of the cells lining the convoluted tubules was found to be homogeneous and granular; and the cell-body was in some instances enlarged to such an extent that the lumen of the tubule was occluded thereby. The line of demarcation between individual cells was obscured and sometimes obliterated. In the severest fatigue vacuolization of the protoplasm was seen, and a certain number of cells showed extreme degeneration, resulting in rupture of the cell-body, the lumen of the tubule being filled with detritus composed of cell-fragments with here and there a normal nucleus or small granular masses which stained like nuclei. Similar changes were present in the liver-cells though not to so great a degree, the distinctive feature in the cells of this organ being the large quantity of bile-pigment contained in them.

## THERAPEUTICS.

**Action of Phosphorus on Blood of Birds.**—The administration of small, non-fatal doses of phosphorus to chickens, according to J. Vogel (Arch. internat. Phar. et Thér., vol. x, fasc. III, IV) causes a diminution in the number of red cells, noticeable by the second day and reaching its acme from the third to sixth when the counts show half or less of the normal. The hemoglobin is reduced proportionally, and no free pigment is found in the serum or the excretions, though they often contain biliary coloring matter. If the phosphorus is stopped normal figures will again be obtained in about eight days. Since the total amount of blood suffers no change, the reduction cannot depend upon a dilution, but a destruction of red cells must take place.

**Treatment of Diabetes.**—The proper dieting is of the greatest importance in the treatment of diabetes, according to H. Eichhorst (Ther. Monatsh., September, 1902), and he even goes so far as to state that no drugs have much influence on the process. The good effects derived from a stay at some watering-place again must be ascribed to the diet, which should consist exclusively of fat and proteid. In saccharin we possess an excellent substitute for sugar, and one which can be taken for years with impunity. Dulcin or sucrol is not so sweet, and is more liable to have disagreeable after-effects. Despite the many preparations on the market, the proper substitutes for bread have not yet been found, for those which have been tried either become disagreeable to the taste after a while, or they are too rich in carbohydrates. If the condition permits the use of any bread at all, Graham bread is to be preferred. One should never forget that the diabetic needs more actual food than the well, since he loses so much, and underfeeding should be avoided. As with morphine, it is generally better and more agreeable for the patient to withdraw the forbidden articles of food slowly than rapidly. The scales should be used freely to control the body-weight. If the urine has been free from sugar for several weeks small quantities, say 25 grams, of bread daily are permitted, and the amount is increased daily 10 grams till 70 to 100 are reached, which is sufficient for most. As soon as traces of sugar again appear the bread must be re reduced in some, and in others entirely withdrawn. The author has never seen any good from gland preparations.

**Value of Yeast of Commerce.**—That yeast possesses some value in diseases of the skin, notably in furunculosis, is beyond question. The many negative reports are due to the inefficient preparations employed. It thus becomes necessary carefully to test all yeast, and R. Rapp (Münch. med. Woch., September 9, 1902) has investigated five widely employed preparations for the amount of water, fermentative, digestive and bactericidal powers and number of bacteria contained. The astonishing results obtained were that most samples were inefficient for therapeutic purposes, and only one, zymin, prepared by dehydrating in aetone, really comes up to the standard.

**Atropine in Ileus.**—For cases of intestinal obstruction, P. Ostermaier (Münich. med. Woch., September 9, 1902) recommends that small doses of atropine be in-

jected in half-hourly doses until 10 mg. are used. If the desired result has not taken place six to eight hours after the first injection the only hope lies in an operation. How the atropine acts on peristalsis is not settled, but it is probable that it stimulates it and diminishes the caliber of the mesenteric vessels. At the same time, however, excessive peristalsis or spastic conditions of localized intestinal areas can be relieved. The circulation is materially improved, and the patients generally rapidly come out of their collapse under the atropine treatment, and there is no obscuring of symptoms as is seen with opium.

**Case of Formalin-Poisoning.**—A. Gerlach (Münch. med. Woch., September 9, 1902) was suddenly called to a patient whom he found breathing stertorously and in deep coma. Since there was a suspicion of poisoning, the stomach was rapidly washed out, and the odor made it clear that formalin had been swallowed by mistake. On the following day the coma still persisted, and since no urine had been passed, a catheter was inserted, but only three or four drops of a dark fluid could be obtained. Diarrhea soon followed, and consciousness began to return slowly. Respiration, pulse and temperature now were normal, and the patient began to complain of much vertigo and burning in the throat. The urine came more freely. It contained traces of albumin and formic acid, but soon became normal after large amounts of water and milk. The local effects upon the digestive tract rapidly subsided.

**Effect of Levico Water on Metabolism.**—In experiments on himself, E. Schreiber (Münch. med. Woch., September 9, 1902) has studied the effects of small amounts of arsenic, such as are contained in the well-known Levico water, on general metabolism. His body-weight did not change, but there was a marked saving of nitrogenous principles, since considerably less nitrogen was excreted through the urine and the feces. The exceedingly favorable reports which have followed the use of Levico water may well find their explanation in the power it has to permit the full use of the ingested proteids.

**Action of Ferric Perchloride in Erysipelas.**—Iron is almost always given as routine treatment in cases of erysipelas, but few physicians even pretend to know what action it has upon the course of the disease. A very ingenious theory is offered by J. G. Drennan (Med. Rec., September 6, 1902), who suggests that it is not given for its hematinic action. The circulation being obstructed in the diseased area, the ferric chloride will not enter this area, but circulates in the vessels just outside of it, and exudes from the capillaries into the tissues in which they lie. Iron exerts its action by diminishing the size of the vessels by pressure from without. This action of iron increases a clotted or unsuitable area in which any bacteria that have so far escaped being entangled are prevented from advancing into new fields. Since it requires large doses of the drug to produce these effects, it is useless to depend upon tonic doses for good results.

**Ipecacuanha Alkaloids.**—Two alkaloids of this time-honored drug are now prepared and on the market; namely, cephaelin and emetin, and there is a gain in the accuracy of the physiological results and of satisfaction in therapeutic application. There are various differences between the alkaloids, especially as regards the emetic dose, and the question is probably not at the present time settled as to just which is more preferable for a given patient. R. B. Wild (Lancet, September 6, 1902) has an article on this subject which contains the following points. For the purpose of comparison, solutions of the different salts were prepared in water and in different strengths of alcohol. Half of each solution was used for clinical purposes; the other half was set aside and examined from time to time as to its keeping properties and activity. Some of the solutions the author has now kept for several years, and they are still active. It is, however, not advisable to expose them to a strong light. Cephaelin hydrochloride was soon found to be less suitable for the ordinary uses of ipecacuanha in catarrhal conditions and bronchitis than the emetin salts. The emetic action of cephaelin is so powerful that it is very difficult to regulate the dose so as to obtain any effect at all without causing nausea and sickness after a few days' continued use. In one case in an adult he found that even .01 gr. every four hours produced nausea and vomiting within three days. At the same time the effect upon the secretions of the nose and respiratory tract and the depressing action on the pulse were less marked than could be obtained by doses of emetin which caused no sickness. Another reason for preferring emetin to cephaelin was that the salts of the latter appeared to be less stable, since the solutions after a time became of a brownish-yellow color, while those containing emetin and kept under the same conditions were still colorless. He has not been able to distinguish any difference in the mode of action or keeping properties of the two salts of emetin which were used; namely, the hydrochloride and the hydrobromide. The solutions of these salts in 20 per cent. alcohol have remained uncolored, clear and active for several years, and there seems no reason to doubt their permanence within reasonable limits of time. Pharmaceutically, in the specimens the author has obtained, the hydrobromide appeared the purer salt, as it was whiter and better crystallized. The solutions first employed were one in 100, and proved too strong for convenience, as the expectorant dose was one to three minims for an adult. Solutions of the strength of one in 1,000 were then prepared, but though satisfactory in their action, the dose was inconveniently large, especially for emetin purposes. The one in 1,000 solution of emetin hydrochloride does not, in the author's experience, quite equal in activity freshly made vinum ipecacuanhæ, which is standardized to one in 1,000 of total alkaloids. During the last two years this authority has used a solution of emetin hydrobromide in 20 per cent. alcohol containing one gr. in each fluid ounce. This solution has proved very satisfactory, as it has remained unchanged up to the present time, is very active and reliable, and the dose is of convenient size; namely, for adults, five to 20 minims for expectorant and depressant purposes, and from one to three dr. as an emetic. He has also used a solution containing one in 100 of morphine hydrochloride and one in 500 of emetin hydrochloride as a sedative and diaphoretic in place of Dover's powder, but has not been entirely satisfied that the action of the solution in equivalent doses is equal to that of the powder. At present comparison is being made between a solution containing one in 500 of emetin hydrochloride and one in seven and one-half of liquid extract of opium and another solution containing one in ten liquid extract of ipecacuanha and one in 100 of morphine hydrochloride. It is still too early to draw any conclusions as to the relative value of the pure alkaloid and crude drug in either case. Wild says that his clinical opportunities for observing the therapeutical effects of emetics are so few that he has been unable to test sufficiently whether cephaelin possesses any properties (especially absence of circulatory depression) which will enable it to compete successfully with emetin and apomorphine as an emetic. Unless clinical observation reveals such properties there does not seem any special indication for the use of cephaelin, since even the emetic dose of the emetin salts is small enough for all practical purposes.

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## THE NEED OF AN AMERICAN "D.P.H."

AN English writer has declared that "sanitary instruction is even more important than sanitary legislation." This belief has been translated into British practice by the establishment of courses of instruction in sanitary science leading to the diploma in public health—the "D.P.H." which the applicant for a position in the public health service of England is expected to acquire as a preliminary to his candidacy.

From time to time efforts have been made to induce the legislature at Albany to grant State aid towards the foundation in this State of a school of public medicine. The failure of these efforts does not signify that the legislature is either hostile or indifferent. The proposed school could be established most advantageously in connection with an existing university, and a stumbling-block to legislative aid is encountered in the demand that one university be favored to the detriment of its rivals.

The need of an American "D.P.H." is pressing; whether public funds are or are not provided for the purpose, it is high time for the introduction of comprehensive courses of instruction in state medicine. In the near future, departments of health, national and local, will compare in importance and dignity with any governmental agency for the promotion of the general welfare. The progressive application of the ever widening principles of sanitary science demands training which our medical schools do not now provide. In England the candidate for "D.P.H." is instructed in the statute laws relating to public health, and he becomes familiar with the adulterations and contaminations of food, as well as with the means for their detection. He studies water-supplies and their regulation; the principles of hospital, dwelling and factory construction, ventilation, drainage and sewerage; the problems of school hygiene, trade nuisances, the diseases of animals in relation to the health of man, methods of dealing with epidemic contagious diseases, meteorology and vital statistics. The mere enumeration of these branches of instruction suffices to make evident our own need.

The functions of the modern board of health are legislative, judicial and executive. Not all branches of sanitary work demand medical training, but for many such training is indispensable. It is a mistake, however, to suppose that the control of departments of sanitation will remain generally in the hands of physicians without any effort on the part of the profession to retain such control. The education of the physician furnishes the best foundation for such work, but it must not be forgotten that the engineer, the chemist, the bacteriologist, are also in the field. In large centers of population the cooperation of these experts is necessary. They, no less than physicians, are men of general education and broad ideas, and their claims to leadership will command increasing respect if superior technical training is not made available for their medical rivals.

A recent work on municipal sanitation, from the pen of an engineer, declares that *"the bacteri-"ologist, the chemist, the engineer, the intelligent "school principal, and a growing body of laymen, "understand the need of health protection and "the methods necessary to that end, quite as fully "as the physician, while their grasp of the sub-"ject is often more comprehensive and more in "accord with modern ideas."* There is an element of truth in this statement. The training of non-physicians in state medicine is not superior to that of physicians, but it is not greatly inferior. While our opponents have not much to boast of, they gain in strength because of our weakness. Medical schools must bestir themselves. If an American medical "D.P.H." is not soon provided the profession will find an important class of public positions slipping from its grasp.

## THE OUTWARD VISIBLE SIGN OF THE INWARD SPIRITUAL GRACE.

THAT the size and measurements of the skull have a direct bearing on the intellect of the owner has been a popular belief since the days of Gall and Spurzheim, and on it are founded many of the misconceptions and fallacies of phrenology. Old as this rock of ages is, however, it has, under the attacks of science, cleft to a degree sufficient to let in the light of modern research, and beyond the facts that a square jaw is associated in our minds with determination, that a receding forehead is supposed to be indicative of ferocity, while a large occipital protuberance points to a fully developed but unplatonic fondness for the opposite sex, little has been accomplished to the credit of its devotees.

It is true that we can measure the skull in various planes and diameters, as has been done at the West Riding Asylum in England, and thus determine that the average of the circumference of the head in insane persons is practically the same as in the sane, and that seven and one-eighth inches is the size of the most commonly accepted hat; but we cannot indicate *degrees* of intelligence by figures any more than in our childhood days of mental arithmetic we could divide apples by oranges. Again, the inner surface of the skull hardly corresponds with the outer, and an exostosis might give a most startling variation to our measurements, when it would and could produce no effect on the contents of the cranial cavity. Notwithstanding this, some years since an expert for the Government in the trial of the assassin Guiteau, after exhibiting diagrams of the heads of many prominent people, culled from the *conformateur* of a local hatter, introduced a series of dimensions of the prisoner's head, obtained by measurements with flexible metal tubing. Any possible effect, however, that this might have produced on the jury was nullified by the defendant's rather irreverent but altogether pertinent characterization of the whole proceeding as "a lead-pipe cinch!"

According to Cosmos the question, "Is intelligence connected with cranial capacity?" has often been brought up by scientists, but their investigations have resulted in nothing, and this has generally been regarded as due to the fact (which we have already pointed out) that these "two magnitudes are incommensurable," as variations of intellect can hardly be mathematically expressed. In spite of these difficulties, and apparently undaunted by them, Professor Karl Parsons has proved the courage of his convictions by a series of experiments that he describes in a comparatively recent paper read before the London Royal Society. In order that the results of an examination of a considerable number of people might not be affected by a difference in age, sex and previous condition, he selected a homogeneous group of students, undergraduates in Cambridge University, where not only the environment would be the same, but where he could obtain from the college authorities the scholastic standing of each, and thus to a degree compare the outward visible sign of the head with the inward spiritual grace of its contents. The Anthropological Society of Cambridge agreed, it seems, to furnish the measurements made on a system invented by the professor, but what the system was, beyond the fact that it was "his own," does not appear. That it was not a "poor thing," however, seems probable from these facts: (1) From the days of perpetual motion to those of its understudy, the Keely Motor, all startling inventions have been shrouded in professional mystery, and (2) the results obtained from examinations in other colleges and universities in the United Kingdom agree in bringing out the combined conclusion "that the intelligence of a student, so far as it can be measured by his success as a scholar, has no sensible relation to the size of his head." This also confirms the statement of another "professor," this time an American, the late Brother Jasper of Richmond, who a decade ago insisted that it was the sun and not the world that moves; as a proof of which we find ourselves, after a generation of experiment and endeavor, still clinging to the aphorism of the past: "Small head, little wit; big head, not a bit."

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## INCREASE OF PHYSICIANS.

THE rosters of the medical colleges of the United States for the educational year just opened show already that there is to be an increase in the number of medical students over those registered in previous years. Notwithstanding the fact that practitioners all over the country have been complaining for some time that there is so much competition in professional life as to make the earning of a suitable living very difficult in many cases, there has been for many years a constant increase in the number of those applying themselves to medicine.

It is well known that a large number of those who graduate from medical colleges do not continue in the practice of the profession. At least

one-third of all medical graduates, it is said, take up some other occupation in life. In recent years the number of physicians who have found it advisable to turn to other pursuits has been larger than ever. As brokers and real-estate dealers many have found a much more lucrative occupation. But even this factor has not relieved the stringency of the situation to any marked extent.

It would seem wise then for family physicians generally to discourage more frequently than they do at present the taking up of the study of medicine by the young members of families to whom they stand in the position of advisers in more than purely medical matters. The value of medical education as an intellectual training is scarcely of sufficient importance to justify the thought that the years spent at medicine will anyhow prove of equivalent value to almost any other form of development. The feeling that men who have had a medical education will at least know how to take care of their personal health is entirely erroneous. Physicians are well known to be as a rule extremely careless of their health, and their want of even ordinary watchfulness in this matter is self-confessed in their own ironical question, "What is the use of being a doctor if you can not neglect your own health?" As a matter of fact ex-physicians and ex-medical students make the worst possible patients, and exemplify very well the proverb that "a little knowledge is a dangerous thing."

While in America the number of medical students is increasing, on the Continent the medical profession is congratulating itself on the lessened registration in the medical schools during recent years. La Semaine Médicale for September 3, 1902, publishes the statistics of medical-student registration in Germany and France for the last five years. In 1897 there were 8,317 men and women registered as medical students in the various universities of France. In 1902 the number was but 7,882, a decrease of 435 or nearly 5¼ per cent. In the same five years there was a reduction in the number of German medical students from 8,141 to 6,749, making it 1,392 less in 1902 than in 1897, or more than 17 per cent. It must be remembered that Germany has a population of nearly 55,000,000, while France has scarcely 35,000,000. Moreover, all students of medicine in Germany must be on some university register, but a large number of French medical students—nearly one-fourth, La Semaine Médicale says—while doing special hospital work are not enrolled. The reduction in France is then probably not even as great as has been announced.

Present industrial conditions in Germany are responsible for the very sensible state of mind that has brought on this eminently desirable decrease of prospective physicians. The development of many great industries calling for special knowledge of applied science has opened up a large number of careers for young Germans in which the immediate rewards are much better than in the professions, and the eventual prospects of great prizes for the specially successful at least as good as in any other condition in life. A corresponding industrial development has not taken place in France, and hence the overcrowding of the profession continues much greater than in Germany. In the United States, however, industrial conditions are quite as good as in Germany, and it is time to look for a like effect in the reduction of professional aspirants.

How undesirably crowded the medical ranks can become is well seen in some statistics of the number of European physicians to the population published recently by the Zeitung für Social-Wissenschaft. In Germany the number of medical practitioners to every thousand of the inhabitants is five and one-tenth, while in France, despite the proportionately and even actually larger number of medical students, it is not quite four to the thousand. The English-speaking countries of Europe have the highest ratio of physicians to inhabitants, Scotland having nearly eight, England over six, and Ireland nearly six per thousand of population. Spain has more than seven physicians to the thousand inhabitants, Switzerland and Italy slightly more than six, while Sweden, Russia and Hungary have less than three per thousand.

In the United States the average number of physicians in the different States is not yet as high as in the most highly civilized European countries, but in some of them it approaches nearly to the general average on the Continent. New York and California have each nearly three physicians to every thousand inhabitants, and most of the States have more than two per thousand.

Old physicians used to say that at least five hundred persons were required to provide a reasonable living for even a young doctor. Recent graduates were advised never to settle in a town of less than a thousand people if there was already a physician in practice, unless there was good prospect of an immediate increase in the population. Curiously enough the proportion of physicians to the population in the large cities is not greater than in the immediately neighboring coun-

try. In New York, for instance, there are practically as many physicians to the number of inhabitants in the State outside of Greater New York as in the metropolis itself. This makes even clearer the necessity for limiting, as far as it can be done by legitimate attention to the best professional interests, the number of those about to enter upon the study of medicine. The increasing severity of entrance regulations and length of studies required will do much in this matter, but the personal influence of physicians can and should be exerted so as to secure only select candidates for medical professional ranks.

## ECHOES AND NEWS.

### NEW YORK.

**Harlem Hospital.**—The Board of Estimate has appropriated the sum of $220,000 for the new Harlem Hospital.

**Dr. Van Valzah Resumes Practice.**—Dr. W. W. Van Valzah has resumed professional work in partnership with Drs. Nisbet and Hayes.

**Kings County Medical Society.**—At the last regular meeting of this society, held Oct. 14, Dr. James J. Walsh of New York read a paper on Rheumatism and Pseudorheumatism. It was fully discussed by Drs. Bierwirth, Fuhs and Morton.

**What is the Medical Profession Coming To?**—On the ground that the death of his seven-year-old daughter Gertrude was indirectly due to improper diagnosis of her disease, John P. Purcell of New Dorp, S. I., was awarded in the Richmond County courthouse, at Richmond, yesterday, a verdict of $500 damages against a reputable physician of New Dorp. The case was founded on a supposed confusion of bronchial pneumonia and diphtheria. With courts that will sustain almost every form of quackery, the question might well be asked, Has the reputable practitioner any rights?

**The Religious Anti-Drug Society.**—The Rev. W. N. Richie, D.D., a Presbyterian clergyman with an office in the Presbyterian Building, and who is secretary of the Interdenominational Committee for the Cure of the Drug Habit, of which, according to his circulars, the Rev. R. F. Sample, former Moderator of the Presbyterian General Assembly, is president, has been found guilty in Special Sessions of practising medicine illegally. He was fined $75. The New York County Medical Society was the complainant in the case. For the last three years Dr. Richie, according to the complaint in the case, has advertised a cure for the drug habit. According to circulars and pamphlets which he sent out the Interdenominational Committee was formed for the purpose of receiving donations for the curing of victims of the drug habit by Dr. Richie's remedy. The treatment was for those in impoverished circumstances, who could not afford to procure the remedy themselves. Dr. J. D. V. Young of the County Medical Society said that the society had had its attention first called to Dr. Richie's work last August. Dr. Young said that complaint had been made that Dr. Richie was not a licensed physician and that he was consequently violating the law of this State by prescribing for those who came to him. "Dr. Richie," according to Dr. Young, "did not have the right to prescribe a cure for the morphine habit. A druggist has the right to sell patent medicines or any other medicines to those who call for them, but unless he has regularly passed his examination as a physician the law says he cannot prescribe any remedy. That was what Dr. Richie apparently was doing. He was prescribing his own remedy, according to the complaints we received, and as a clergyman he had no right to do that, no matter how efficacious it might be."

### PHILADELPHIA.

**Obstetrical Society of Philadelphia.**—Dr. F. C. Hammond has been elected secretary of this society to succeed Dr. Frank W. Talley.

**Decrease in Contagious Diseases.**—For the week ending Oct. 11 there were but 55 cases of typhoid fever, as compared with 100 the preceding week. But one case of smallpox was reported.

**Philadelphia Hospital Nurses Graduate.**—The annual commencement of the Philadelphia hospital training school for nurses was held Friday evening, Oct. 10. Addresses were made by the mayor and by officials and physicians of the institution. The graduates numbered 24.

**Books Not Medium for Spreading Disease.**—The librarian of the Philadelphia Free Library believes that the chances of spreading disease by the circulation of books from a public library are very slight. He states that for every book touched by a reader there are fully 100 handled by employees of the library, among whom, in spite of this, there has not been an instance of contagious disease since its beginning. When one of the volumes is found in a house where there is a contagious disease it is destroyed by the physician in charge, this being by order of the Board of Health. Less than 200 books a year are lost in this way.

**Report of State Board of Health.**—The seventeenth annual report of the Pennsylvania State Board of Health, just issued, contains references to many items of interest to the profession. The report contains the first complete list of township school boards of health authorized by the legislature in 1899. There are now 20 of these in operation. During 1901 there were established 19 town and borough boards of health. The report states that it is yet to be demonstrated that vaccine virus ever contains or becomes contaminated with the tetanus bacillus. As tetanus could not logically be said to follow vaccination unless the germs of that disease be introduced into the wound, the board states that no person need fear vaccination on that account. The need of this preventive of smallpox is urged. Lists of the points in the State where smallpox has occurred are given. During the year the assistance of the board was required at 29 points for the suppression of diphtheria, as against 38 in 1900.

**For Medical Defense.**—The Philadelphia County Medical Society has under consideration certain plans for aiding its members in meeting suits and threats against them and also for assisting in prosecuting illegal practitioners. The plan calls for the appointment of an attorney for one year to conduct suits for the society and to assist the district-attorney in stopping illegal medical practice. The directors of the society will assume charge of suits for malpractice brought against members, if the censors decide that the claim is valid. This does not apply to suits arising from any affair happening before the person became a member of the society. The directors will have sole authority to handle the case by defending the claim or by compromising, except when the member in question is also a member of other protective associations. The society is not bound to the payment of damages awarded. It is probable that the annual dues will be raised in order to insure a sufficient fund to carry out the above scheme.

**Nervous Symptoms in Chronic Nephritis.**—At a recent symposium on nephritis at the Philadelphia County Medical Society Dr. J. Hendrie Lloyd said that it was obligatory for the neurologist to make himself familiar with the symptoms and treatment of nephritis. Symptoms may be divided into regional and general. Special peripheral parts do not suffer markedly but the general involvement may make up a symptom-complex not unlike that found in other conditions. Regional symptoms were dwelt upon particularly. Headache as an early symptom of nephritis is of great importance. Though not common it is very often overlooked in the cases in which it does occur and treated with every coal-tar product known before it is finally diagnosed. Headache is rarely a truly isolated symptom. A pseudomigraine late in life should lead to suspicion of either nephritis or cerebral disease. In some of the cerebral manifestations of nephritis a difficult diagnostic problem is involved, although uremic encephalopathy includes more than convulsions. There is nothing absolutely distinctive about the convulsions and coma of Bright's disease. The diagnosis must be made by exclusion, by examination of the urine, etc., and then it is still difficult. Subnormal temperature as a sign of uremic coma is unreliable. Attention was called to the simulation of organic brain disease (tumor, etc.) by nephritis.

**First Medical Book Written and Published in America.**—A recent number of the Philadelphia Press contains, in an article on the College of Physicians, an interesting account of the first medical book written and published in America. The College possesses the only known copy of the first edition of that work, and also the original manuscript notes of it. The author, Dr. Thomas Cadwalader, freshly returned from studies in London, embodied in the book the results of his studies concerning lead colic, or "Dry Gripes," as it was popularly called. This disease, which he characterizes as "a cruel distemper," was especially prevalent because of the consumption by Philadelphia's population of large quantities of West Indian rum made by distillation through leaden pipes. Dr. Cadwalader took his notes on the disease with him to Trenton, where in 1745 he wrote the book in question. As if expecting criticism of his book he inserted a paragraph explaining how Horace distinguished a critic from a caviller. Thinking better of this after a few copies of the book had been printed, the reference to critics was left out of the remainder of the edition. The following from the preface gives a glimpse of a state of affairs that is rather refreshing during the present almost universal craze to rush into print: "I have long been of opinion that 'tis the duty of physicians to frankly communicate to the world any particular method of treating diseases which they have found to be successful in the course of their experience and not generally known or practised by others. By this the medical art has been and may still be improved. Many are the advantages the present age reaps from such disinterested conduct in our predecessors; and when we have freely received, surely we should freely give."

**The Treatment of Nervous Phenomena in Chronic Bright's Disease.**—Dr. J. M. Anders spoke on this subject, discussing first the general treatment of the disease. A suitable diet for individual cases must be selected, as a routine method in this regard will not do. An absolute milk diet in the presence of gastric irritability or during acute exacerbations of the attack is advisable, but at other times this should not be the sole food. When given alone milk furnishes an abundance of carbohydrates, and the patient also develops general weakness, both of these being undesirable. For these reasons a mixed diet is better. An abundance of fluids should be given. The treatment of nervous symptoms is purely symptomatic. In cases of coma use croton oil, the hot pack and pilocarpine, with strychnine and digitalis to support the heart. Blood-letting may be finally resorted to. When nervous convulsions are present treatment is governed by the state of arterial tension, venesection often being especially serviceable. The working rule in these cases should be, "When in doubt, bleed." Cardiac stimulants are demanded if that organ shows signs of weakness after bleeding. These consist of digitalis, strychnine, strophanthus, and camphor hypodermically. The general opinion is that opium aggravates the tendency to uremia. When venesection and jaborandi have failed, opium may be tried, in chronic cases only. The value of chloroform in cases of convulsions is much exceeded by free bleeding. To relieve arterial tension in chronic cases nitroglycerin, potassium iodide, or sodium nitrite may be exhibited. The use of this last drug has been greatly neglected by physicians. For the headache of Bright's disease, generally only temporary relief can be secured. The combination of phenacetin and caffeine has given Dr. Anders much satisfaction in the treatment of this annoying symptom.

**Hemopericardium Simulating Mediastinal Tumor.**—Dr. David Riesman reported this interesting case at the October meeting of the section on medicine of the College of Physicians. Hemopericardium as generally recognized is an acute condition and is fatal or accompanies a fatal disease. The case in question would seem to indicate that there is a chronic form and also suggests the possibility that such a form may be amenable to treatment. The patient was a male, aged thirty-eight, a worker in a rolling-mill. Symptoms began five years before admission to the hospital and had been marked for the last two years. For five months he had not been able to work. There was dyspnea, expectoration, dryness of the throat, bad taste in the mouth and marked distention of the veins. There was absolute flatness over a large area continuous with the heart-dulness, this extending two inches to the right of the sternum at the level of the fourth rib. Auscultation revealed loudness of the heart-sounds, which were transmitted to the right and heard over the area of flatness as well as at the usual site. Wheezing râles were heard over the chest, and there were some signs of pneumonia posteriorly. The pulse was 90. Cyanosis was present, as was edema of the feet and afterward of the arms. The diagnosis of mediastinal tumor was made. By means of a needle a reddish fluid containing red and white blood-cells was obtained. This was regarded as another evidence of new growth. A second tapping was proposed, but was abandoned because of fear of a possible aneurism. Autopsy revealed a hemopericardium with no apparent cause for the effusion. The kidneys showed only cyanotic induration. One of the points emphasized by Dr. Riesman was that a pericardial effusion does not necessarily eliminate the sounds of the heart, this case showing that they may be preserved and even increased. The intensity of the sounds probably depends more on the vigor of the heart-muscle than on the quantity of the fluid present. The rational treatment of these cases is tapping. The question regarding the propriety of injecting iodine for the cure of recurrent hemopericardium arises. Dr. Riesman thinks this expedient would be worth trying. Points brought out in the discussion were the frequency of the signs of pneumonia posteriorly in cases of pericarditis, and the not infrequent mistake of diagnosing pericarditis with effusion when the condition is that of acute dilatation of the heart.

## CHICAGO.

**Commencement Exercises of Rush Medical College.**—At the convocation of the summer class of Rush Medical College 20 students were graduated. The doctorate address was delivered by Dr. Norman Bridge.

**Opening Exercises of Northwestern University Medical School.**—These exercises occurred Oct. 7, when an address was delivered by Dr. Henry Gradle, entitled "A Glimpse Into the Future of Medicine." It is said that the registration so far is larger than in any previous year. Dr. F. Robert Zeit will take the chair of pathology for the year in the place of Dr. A. P. Ohlmacher, who has resigned.

**County Institutions.**—The County Board of Commissioners has decided to submit to the voters, at the election next month, a proposition to issue $500,000 in bonds, of which $350,000 is to be devoted to the remodeling of the insane asylum and hospital at Dunning, building additions thereto, and also erecting a group of cottages for consumptives, and $125,000 for the erection of a ward for epileptics, a ward for contagious diseases, and a ward for alcoholic cases at the County Hospital.

**Surgical Treatment of Hemorrhagic Pachymeningitis.**—Dr. John C. Munro of Boston read a paper (by invitation) before the Chicago Medical Society, Oct. 8, on this subject. He drew the following conclusions: Alcohol, syphilis, acute and wasting diseases and trauma apparently bear some causative relation. The symptoms are those of acute subdural hemorrhage coming on slowly, producing mental irritation, spasm, rigidity of the extremities, convulsions, and later on paralysis, the sequence being more or less irregular. The treatment is surgical, and should be instituted as early as possible. Without operative relief, in cases where pressure symptoms manifest themselves, the prognosis is practically hopeless. Early operation gives the best chance for recovery.

**Hospital Ordinance.**—Recommendations regarding the provisions of the proposed hospital ordinance have been made to Commissioner of Health Reynolds by Medical Inspector Hunt. He urges that the license fee be increased from $10 to $250 a year, and that the consent of the owners of two-thirds of the frontage in the block involved and on the nearest sides of the adjoining blocks be required. Under the present law an organiaztion desiring to establish a hospital anywhere in Chicago must obtain the consent of all the individuals owning property in the entire block in which the hospital is to be located, and also the consent of all property owners on the opposite side of the street on which the hospital is to face. This makes it impossible to build a hospital and obey the ordinance, unless the hospital is to be placed away out on the prairie. The trouble with the frontage consent requirement is that it enables some property owners to hold out and blackmail those proposing to set up a hospital. Chicago is particularly fortunate in her system of hospitals, which is not excelled by that in any other American city. The proposed changes to the hospital ordinance are now in the hands of the health committee, and pending its report of a bill containing its recommendations the city council has relieved the hospitals until Jan. 1 from the operation of the clause requiring frontage consents in the present ordinance.

**Hydrotherapeutic Treatment of Typhoid Fever.**—Dr. Henry B. Favill spoke on this subject. The statistics in favor of the bath treatment were favorable as compared with other forms of treatment. He referred to the typical, original Brand bath, which he defined as the vigorous rubbing and manipulation of the typhoid patient, well immersed in water of a temperature varying from 60 to 80° F. The manipulation of the bath is an essential part of the process; the temperature is subject to variation. Although the antipyretic value of the bath is important, he considers it a mistake to centralize attention upon its antipyretic effects. Its effect upon the patient is sedative and tonic. A patient who is subjected to an intelligent administration of a cold bath in typhoid, typically and regularly, shows marked sedative effects, as manifested, first, by a feeling of comfort, as against a previous feeling of malaise; second, as manifested by a tendency to sleep, as contrasted with previous restlessness and inability to sleep. The second phase of the bath was its tonic effect, as manifested by an improvement in the cerebral condition, a condition of clearness of mind as against hebetude; of alertness as against indifference; of comfort, physical and psychical, as against distress. This was a fair index of improved tone. As to the digestive tract, there was typically a better digestion, as evidenced by the decidedly less typhoid character of the tongue, and by a less tendency to meteorism. He described a modification of the Brand method for use in hospitals and in private practice.

**The Dietetic Management of Typhoid Fever.**—Dr. Frank X. Walls read a paper on this subject. He paid particular attention to "milk alone," saying that it was objectionable as a typhoid diet: (1) Because it is intolerable as a sole food for the adult in health or disease; (2) it contains a large amount of poisonous filth; (3) in digestive tract infections it feeds the parasitic intestinal flora rather than the hose; (4) the systemic intoxication from milk-poisoning is serious and often fatal; (5) we have abundant other substances that are without these objectionable features, and more palatable, equally abundant, very nutritious, easily digested and readily assimilated. How will we feed typhoid patients, for they must be fed, and the successful treatment depends in a large measure upon the attention that is given to the diet? The keynote of the dietetic management is individualization. Water should be given freely, plain or charged. Gruels, well cooked and seasoned, strained and malted, if preferred, made from oatmeal, rice, barley, arrowroot, or other cereals, have a moderate nutritive value. Meat broths or soups of beef, mutton or chicken have a slight nutritive but more stimulant value. Meat juice, made by the cold method, contains from seven to nine per cent. of proteid, and is a good food, and from 5 to 15 ounces may be given a day. White of egg added to water, gruels or soup enriches them. The yolk of the egg is very rich in fat, and, beaten in with cereals, it makes a very palatable, nutritious food. Jellies, calf's-foot or fruit, are a delicate addition. Fruit juices, of orange, grape, berries, lemon or pineapple are tonic beverages that break the monotony of the sameness of a typhoid diet. Cream and milk, but the best only, may be given very cautiously with other foods; given plain, or flavored with malt, coffee, chocolate, etc., acidulated, peptonized, pancreatinized. Koumyss, buttermilk, junket, are nutritious milk foods. This list is merely suggestive, and may be as varied as the needs of the individual require. The concentrated foods are rarely required, though somatose, tropon, plasmon, plasmon coca, or condensed milk are at times of service. Patients should not be overfed. The physician should watch the abdomen for gaseous distention of the bowel, and the stools for evidence of indigestion or food putrefaction. If present, correct the diet rather than administer antiseptic or antifermentative remedies. Alcohol may be used according to the particular indications in the specific case.

**Typhoid Fever in Infants and Children.**—Dr. I. A. Abt reported 90 cases. Referring to the treatment used, the author stated that a large proportion of the

cases ran the entire course of the disease without receiving any drugs. Patients were kept in bed and, as nearly as possible, absolutely quiet. They were encouraged to change their position in bed frequently. This enforced rest in bed could not be strictly adhered to in young children. It was necessary to pick them up on account of restlessness, or to change their napkins, and for their baths. The mouths were kept scrupulously clean by washing with boric acid solution. The usual precautions concerning the prevention of bedsores by rubbing the back with alcohol were practised. During the febrile period the patients were kept on a liquid diet, consisting almost exclusively of milk, except in those rare cases where milk could not be borne. After the temperature had fallen to normal, strained gruels, broths and fruit juices were permitted. The patients were all encouraged to drink large quantities of water. No solid food was allowed until the tenth day of normal temperature. The treatment of the temperature was hydrotherapeutic. A temperature above 102° F. was treated by tepid sponging; if the temperature rose still higher and was not reduced by the sponging, the patient was placed in a cold pack. In those cases where the fever was not controlled by either of the foregoing, the patient was given a cold bath. He was placed in a comfortable, warm bath of about 90° F. This was gradually reduced to about 80° F. He found it rarely necessary to reduce the temperature of the bath much below this point. At times, however, where the fever did not yield, the bath temperature was reduced to 70 or 75° F. No antipyretic drugs were employed to reduce the temperature in any case. In cases showing nervousness or restlessness, an ice-bag applied to the head sometimes gave relief. At times a small dose of Dover's powder or sodium bromide was given for restlessness and sleeplessness. Constipation was treated by enemata, and cases of severe diarrhea were given small doses of deodorized tincture of opium. In the prolonged cases, which showed the exhausting effects of the disease, where the pulse was rapid and weak, whiskey or brandy was employed, and moderate doses of strychnine were given. Intestinal antiseptics were rarely employed. Complications were treated as they arose on a rational plan. At the close of the febrile period, patients were frequently given a tonic in a routine way, the favorite being the elixir of iron, quinine and strychnia.

**Bulletin of the Health Department, Week Ending Oct. 11, 1902.**—With one exception, the number of deaths—403—reported during the week ending Oct. 11 furnishes the lowest October mortality on record for the city of Chicago. The annual rate was 11.53 per 1,000 of the estimated mid-year population, 1,820,000. In the week ending Oct. 19, 1901—a phenomenally healthful year in all parts of the world—the total reported deaths were 370, and the annual rate was 10.95 per 1,000 of the estimated mid-year population, 1,758,000. There has been nothing in the weather conditions, the character of the water-supply, or any of the other factors affecting the public health to account for this remarkably low death-rate. It must be attributed to the campaign of education against typhoid fever carried on during the last three months, which has led to greater attention being paid primarily to the prevention of that disease, and also to the increased care of health generally caused thereby. The number of typhoid deaths—22—was exactly the same as during the previous week and as in the corresponding week last year, but the duration of the disease in the fatal cases shows that the epidemic is practically at an end and that the continuous pollution of the water-supply has been offset by the precautions taken in its use. During August the average duration of the fatal cases was 18.5 days; in September it was 24.3 days; since Oct. 1 it has been 31 days—one case being of 90 days, one of 74 days and more than half being of a duration which shows that the disease was contracted in July and August. Returns from various hospitals show 11 per cent. fewer cases under treatment at the close of the week than at the close of the previous week. Sore throats have been occurring in various localities, and a large proportion of these are caused by the germs of diphtheria and influenza. The correct and early diagnosis of these infections can only be made by the microscope. The municipal laboratory offers the busy physician every aid in controlling these diseases early in the season. In malignant cases of diphtheria, when membrane can be sent in with the culture, an immediate examination and diagnosis can often be made. Such specimens should be sent in by special messenger and marked "urgent." A diagnosis will be returned to the physician by telephone at the earliest possible moment. Thirteen cases of smallpox were sent to the isolation hospital during the week. Five other cases were found which had run their course under the supposition that they had chicken-pox. Some of these unrecognized cases attended the St. Alphonsius parochial school at Southport and Wellington avenues. All attacked were children ranging in age from one to twelve years, except one twenty-three years old. None had ever been vaccinated. A case of smallpox in a public school could not have resulted in such an outbreak, as these schools are well protected by vaccination. The parochial schools are not so thoroughly vaccinated, and their principals do not make a certificate of vaccination a requisite to school enrolment. The practice is to admit all and some time during the year have the school vaccinated, but certificates in all cases are not exacted, as in the public schools, though the law requiring a certificate of vaccination applies to the parochial school the same as to the public school. Had this law been complied with in the St. Alphonsius school at the beginning of the term the nine pupils from that school now in the isolation hospital with smallpox, would have escaped the disease. Father Boyle, the head of this school, is an able, conscientious man, and the moment he heard of the existence of smallopx in his neighborhood he had his pupils vaccinated. It is doubtful if principals of parochial and private schools know that the law giving children the benefit and protection of vaccination applies to them as well as to principals of public schools. The 14 deaths reported from suicide again call attention to the appalling increase of self-destruction during the last decade. Since the first of the year there have been 321 suicides—an annual rate of 22.6 per 100,000 of population. The rate in 1890 was 12. In order of greatest increase of suicide 10 cities rank as follows: St. Louis, Chicago, Hoboken, Oakland, Cal., New York, Milwaukee, Cincinnati, Newark, New Orleans and Brooklyn. The health department is confirmed by its researches in the belief that this increase of self-murder, like the corresponding increase of pneumonia during the period, is due to influenza, and again urges upon physicians the prompt diagnosis of this diabolical disease and its radical treatment.

## GENERAL.

**Egyptian Medical Congress.**—Major William C. Gorgas, Surgeon, U. S. A., has been designated by Surgeon-General O'Reilly to represent the United States at the first Egyptian Medical Congress, which will meet in Cairo on Dec. 16. The purpose of the Congress is to collect data in regard to tropical diseases and discuss means for eradicating them.

**Christian Science Again.**—The Arlington Chemical Company have just issued a pamphlet reprint of a

series of short lectures delivered by the Rev. Andrew F. Underhill of St. John's Episcopal Church, Yonkers, entitled "Valid Objections to Christian Science," which is at the same time both interesting and instructive. The profession cannot fail to appreciate these efforts in trying to disseminate sensible ideas regarding this so-called religion,

**Interstate Reciprocity in Medicine.**—It is reported that 30 States are to unite in common laws to regulate the practice of medicine in the United States. This announcement was made to-day by the State Board of Medical Examiners. Hitherto Wisconsin, Indiana, Michigan and Ohio have had an agreement that any physician authorized to practise in any of these States is not barred from any other, as all the States have practically identical laws.

**Treatment of Scarlet Fever by Serum.**—At the seventy-fourth annual meeting of the Deutscher Naturforscher und Aerzte recently held at Carlsbad, Dr. Moser of Vienna reported on a serum treatment for scarlet fever which he said had resulted in a reduction of the mortality of 50 per cent. Professor Escherich and Dr. Paltauf of Vienna also spoke in favor of the new serum. At the same assembly Dr. Oskar v. Hovorka reported on a serum therapy for malaria.

**Medical Practitioners in Egypt.**—The number of Greek medical men in Egypt is always increasing, and, of course, the British have increased greatly in numbers since the beginning of the occupation. A list recently compiled at the central office of the Sanitary Department shows that there are now 1,211 medical men of all nationalities in Egypt; 604 are Europeans; 85 hold a Persian or a Turkish diploma from Teheran or Constantinople; 45 are natives with a European diploma, and the remaining 477 are natives educated in Cairo at the one medical shool of the country. The lowest mortality is in the desert districts, and the highest is in the largest towns.

**Oregon State Medical Society.**—The following new officers of the Oregon State Medical Society were elected September 11, 1902: President, Dr. Henry Waldo Coe, Portland; First Vice-President, Dr. F. W. Van Dyke, Grants Pass; Second Vice-President, Dr. J. A. Geisendorfer, The Dalles; Third Vice-President, Dr. J. P. Tamiesie, Hillsboro; Secretary, Dr. A. D. Mackenzie, Portland; Treasurer, Dr. Mae Cardwell, Portland. Councilors: Dr. W. J. May, Baker City; Dr. J. Fulton, Astoria; Dr. Wm. Amos, Portland; Dr. G. F. Wilson, Portland; Dr. C. S. White, Gervais; Dr. S. T. Linklater, Hillsboro; Dr. W. T. Williamson, Salem; Dr. Wm. House, Pendleton; Dr. Ellis, Portland; Dr. R. C. Coffey, Portland.

**Dr. Currie and the Burns Manuscripts.**—It appears probable, says the British Medical Journal, that Mr. Pierpont Morgan's offer to purchase the Burns MSS. in the Liverpool Athenæum Library for £5,000 will be declined. It may be interesting to some of our readers to know that the MSS. formerly belonged to Dr. James Currie, who used them in the preparation of his well-known biography of the poet. Dr. Currie, who was born in 1756 and died in 1805, after an adventurous career in the West Indies and America, studied medicine at Edinburgh and graduated at Glasgow. He settled in Liverpool, where he soon acquired a leading position, not only in medicine but in literature. He was an ardent advocate of the abolition of slavery and a political pamphleteer of some note. He was a pioneer of the treatment of fevers by cold bathing, and urged the regular use of the thermometer in clinical observation.

**American Veterinary Medical Association.**—The thirty-ninth annual meeting of the American Veterinary Medical Association was held at the West Hotel, Minneapolis, Minn., Sept. 2-5, 1902. Dr. J. F. Winchester of Lawrence, Mass., presided. The address of welcome was made by Mr. Wallace G. Nye, Secretary of the Commercial Club of Minneapolis, and was responded to by Dr. Roscoe R. Bell of New York. The President's address, by Dr. Winchester, was in the form of a plea to the profession to take a more elevated position upon all matters pertaining to its interests. The following papers were read: The Hospital Management of Dogs, by Charles Ellis of St. Louis; The Pathogenesis of Equine Pneumonic Emphysema, by A. H. Baker of Chicago; Icterohematuria of Sheep, by M. E. Knowles of Helena, Mont.; External Ulcerative Anovulvitis of Cattle, by John J. Repp of Ames, Ia.; Texas Fever and its Relation to the Live-Stock Interests of Tennessee, by W. C. Rayen of Nashville; Equisetum Poisoning, by F. A. Rich, Burlington, Vt.; Organization of State Veterinary Work, by Leonard Pearson, Phila.; Results of Strict Sanitary Work in Arizona, by J. C. Norton of Phœnix; Malarial Fever in the Horse, by F. Torrance of Winnipeg, Manit.; Hemorrhagic Septicemia in Cattle, by S. D. Brimhall of St. Paul; Poisonous Stock Foods, by N. S. Mayo of Manhattan, Kan.; Barrenness in Bovines, by Charles Schmitt of Dodgeville, Wis.; Differential Diagnosis of Farcy, Furunculosis and Bursattee, by C. C. Lyford of Minneapolis. Other papers were read by title and will appear in the printed proceedings. On Thursday afternoon the members and visiting friends were given an excursion on Lake Minnetonka, and in the evening they were entertained by a banquet at the Hotel Del Otero, Spring Park. The officers for the ensuing year are, President, Dr. S. Stewart, Kansas City, Mo.; Vice-Presidents, Dr. J. G. Rutherford, Ottawa, Can., W. H. Dalrymple, Baton Rouge, La., Dr. E. M. Ranck, Glenolden, Pa., Dr. M. E. Knowles, Helena, Mont., Dr. M. H. Reynolds, Minneapolis, Minn.; Secretary, Dr. John J. Repp, Ames, Ia.; Treasurer, Dr. Wm. Herbert Lowe, Paterson, N. J. Sixty-six new members were elected, making the membership at this time over 500.

**Changes in the Medical Corps of the Navy, Week Ending Oct. 11.**—P. A. Surgeon C. P. Bagg, ordered to the Naval Hospital, Mare Island, Cal.; Asst. Surgeon E. M. Brown, detached from the Naval Hospital, Mare Island, and ordered to the Naval Museum of Hygiene and Medical School, Washington, D. C.; P. A. Surgeon R. S. Blakeman, having been found incapacitated for active service on account of disability incident thereto, is placed on the Retired List of the Navy; Surgeon F. J. B. Cordeiro, detached from the Constellation, and ordered to the Naval Training Station, Newport, R. I.; Surgeon M. H. Crawford, detached from the Chicago, and ordered home, when his resignation will be accepted, voluntarily tendered; P. A. Surgeon M. H. Bucher, detached from the Panther and ordered to the Machias; P. A. Surgeon W. H. Bell ordered to the Yankton; P. A. Surgeon D. N. Carpenter, detached from the Illinois and ordered to the Chicago; Asst. Surgeon T. M. Lippitt, ordered to the Naval Hospital, New York; Asst. Surgeon J. P. Traynor, detached from the Naval Hospital, New York, and ordered to the Naval Museum of Hygiene and Medical School, Washington, D. C.; Asst. Surgeon A. Stuart, detached from the Yankton, and ordered home to wait orders; Asst. Surgeon F. M. Bogan, detached from the Machias, and ordered to the Naval Hospital, Washington, D. C., Oct. 30; Asst. Surgeon F. M. Munson, detached from the Naval Hospital, Washington, D. C., and ordered to the Naval Museum of Hygiene and Medical School, Washington, D. C.; Asst. Surgeon M. W. Baker, detached from the Naval Hospital, Norfolk, Va., and ordered to the Naval Museum of Hygiene and Medical School, Washington, D. C.; Asst. Surgeon H. F. Strine, de-

tached from the Naval Hospital, Norfolk, Va., and ordered to the Naval Museum of Hygiene and Medical School, Washington, D. C.; Asst. Surgeon R. O. Marcour, ordered to the Franklin; Asst. Surgeon H. E. Odell, ordered to the Naval Hospital, Norfolk, Va.; Asst. Surgeon R. E. Ledbetter, detached from the Chicago and ordered to the Illinois; Doctors B. F. Jenness, H. Shaw, and R. H. Michels, appointed Acting Assistant Surgeons, with the rank of Lieutenant, from Oct. 4; Doctor John L. Neilson, appointed an Assistant Surgeon, Oct. 4.

**Health of the Army.**—The report of Surgeon-General Forwood shows that in spite of the changed conditions affecting the army, and the transfer of troops from temperate to tropical climates and vice versa, the health of our military forces as a whole during 1901 was about the same as its average for the preceding 10 years, and considerably better than during 1900. The mean strength of the army was 92,491 men, of whom 81,885 were Regulars, and 10,606 Volunteers. The death-rate from all causes was 19.94 per 1,000, as compared with 22.74 in 1900, and with 11.91 for the preceding decade. In 1900 the death-rate in 341 cities of more than 8,000 population was 18.6 per 1,000; the figures for the army show that even in war time military life is not very much more dangerous than civil life at home. The admissions to sick report in the year covered by the report constituted 1,791.59 per 1,000 of the strength; that is, every man on an average was reported sick one and three-quarter times during the year. The figures of wounds and injuries are curious. Cases to the number of 17,736 were treated; but the largest proportion of these came from the United States and Cuba. The Porto Rico regiment had an admission rate of 147.43; the troops in the Philippines and China, one of 168.33; the command in Cuba had a rate of 351.90, and the troops at home stations one of 250.08. This difference in the rates of troops on active service and those at home is ascribed to what is undoubtedly the fact, that men on garrison duty in time of peace report sick for slight injuries which they would ignore if on active service. From contagious diseases, the army was very free during 1901. There were only 14 cases of scarlet fever, and 1,382 of mumps; and no deaths were due to either of these sicknesses. Twelve men out of 769 who had measles died, and 37 out of 125 who had smallpox. One out of 14 cases of yellow fever resulted fatally. All of these cases occurred in Cuba prior to the precautionary measures taken by Major Walter Reed, Surgeon, U. S. A., as a result of his discovery that the disease was carried by mosquitoes. There were 594 cases of typhoid reported officially, with 78 deaths and five discharges for disability. Gen. Forwood thinks the figures too low, as more than 1,800 cases of fever were reported as "undetermined." The army was wholly free from cholera for most of the year; but Manila and other places in the Philippines suffered from an outbreak of the disease, and during the month from June 15 to July 15 there were 77 cases in the army in the Philippines, 56 of them fatal. Of venereal diseases there were 13,911 cases, an admission rate of 150.41 per 1,000, a bad showing compared with the rate for 1888-1897, the ten years preceding the Spanish war. The rate was lowest in the Philippines, 144.24; in the United States it was 149.96, but in Cuba was 287.28, and in Porto Rico, 309.63. In commenting on these diseases, Major Ebert, Chief Surgeon of the Department of the Columbia, remarks that the habits of the men are not up to the standard existing before 1898, or to what they were under the canteen system now abolished. From the Philippines it is reported that intemperance has increased since the post exchange was abolished. During the year 104 men were killed by gunshots, 46 of them in battle, and 146 men died of gunshot wounds received in battle; 58 men were killed by gunshots inflicted accidentally, suicidally and homicidally. There were 82 deaths from bolo wounds, all, of course, in the Philippines. The health of the army thus appears to have been about normal. The investigations of the army surgeons, and their work towards the prevention of disease continues without cessation. Col. Charles Smart, Assistant Surgeon-General, is on his way to the Philippines to become Chief Surgeon of the division, having been chosen for the post because of his knowledge of cholera and its causes; and it may be expected that the next report of the Surgeon-General will show a better state of affairs in the Philippines than the present one records.

**Obituary.**—Dr. Elvira Ranier, one of the most prominent women physicians in this State, died last week in her home in Oswego in her fifty-third year. She was born at Coldwater, Mich., and was a graduate of the University of Michigan, consulting physician of the Oswego Hospital, and secretary of the County Medical Society.

Professor B. J. Stokvis of Amsterdam has recently died. He was Professor of Pharmacology in the University of Amsterdam and has been known widely as an investigator and teacher.

Dr. Henry Horace Lynch, who practised in Jersey City for 30 years, but retired 10 years ago, died last week at his home, No. 591 Bramhall Avenue. He had been ailing for some time.

## CORRESPONDENCE.

### TREATMENT OF MORPHINISM.

*To the Editor of the* MEDICAL NEWS:

DEAR SIR—I have been requested to write to the MEDICAL NEWS, giving some of my personal experiences with hyoscine in the treatment of alcoholism and morphinism. When hyoscine was first introduced, several physicians became very enthusiastic supporters of its claims as a substitute for morphine, and as a cure for the craze for alcohol. I made several very careful tests of its effects in over a dozen cases of morphinism, and also in a number of alcoholics, then abandoned it as a very unsafe and dangerous drug.

It was given in small doses often repeated, also in large doses at longer intervals, but the effects were practically the same. In each instance the morphine was withdrawn within a few hours, and the consciousness of suffering was obliterated after the first or second dose of the drug was given. In each case delirium with hallucination and delusions of a mild type began after the second or third dose was given, and continued from two to four weeks. Most of the time the patient had stupor, muscular trembling and general relaxation with excessive sweating and irritation of the bowels. The usual withdrawal symptoms noted in morphinism, marked by extreme exhaustion, relaxation and cerebral irritation, were present only in a modified form. The insomnia from hyoscine was less prominent, and the stupor more prolonged and associated with muttering., also with periods of collapse and profound indifference. The muscular prostration was intense and long continued, and the mental feebleness was apparent weeks after the active symptoms had subsided. In each of these cases convalescence was protracted, and the neurotic derangements which followed seem more pronounced and difficult to control.

Hyoscine has been and is used freely in the quack's specifics and "quick-cure asylums," and when the patient becomes delirious and the symptoms alarming,

morphine is given, concealed, and the hyoscine withdrawn. The patient is then told that he is cured and a preparation of strychnine, hyoscine and morphine is given as a tonic for him to continue after leaving the asylum. Later the patient finds it impossible to give up this tonic, then relapses.

Morphine-takers in a comatose, semidelirious state frequently come under my care after having been treated by irregulars or by some specific taken at home. The form of the delirium and the dilated pupils and the peculiar hallucinations are strong indications that hyoscine has been used.

As a substitute for morphine, I believe it to be more dangerous and uncertain than bromide of sodium. From the use of both of these drugs delirium and dementia are almost certain to follow. From my experience it is dangerous treatment to substitute one narcotic for another. In morphinism there are enfeebled brain-centers and profound anemias, both local and general, that are not curable by the use of other equally dangerous drugs. The conditions which follow the withdrawal of morphine are easily controlled in the proper surroundings by many simple and harmless remedies, and it is difficult to understand why alkaloids like hyoscine and others of this nature should be used to accomplish what can be done with less risk and danger. I believe hyoscine to be a dangerous drug in morphinism or alcoholism, and that any extended use will confirm this statement. A prominent physician, a morphine-taker, who tried to cure himself by large doses of hyoscine, died suddenly, and there were reasons for believing that the hyoscine was an active cause. A few fatal cases of this kind have come under my observation, and while it is impossible to say that hyoscine caused death, there are reasons for believing that it was an active factor in the final collapse.

T. D. CROTHERS, M.D.,
August 20, 1902. Hartford, Conn.

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## THE TREATMENT OF THE MORPHINE DISEASE.

*To the Editor of the* MEDICAL NEWS:

DEAR SIR: Thirty years' experience in the study and treatment of the morphine disease prompts me to protest against a method—so-called—of treating it with "massive doses" of hyoscine hydrobromate, as presented in a paper lately published in the MEDICAL NEWS. It is surprising that one of Dr. Hare's ability should approve of such a plan. It is evident he has much to learn in the treatment of morphinism. There is no place in sound therapeutics for such practice. It is irrational, unscientific, inhumane and dangerous. I warn the profession against it.

J. B. MATTISON, *Medical Director,*
*Brooklyn Home for Narcotic Inebriates.*

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## TRANSACTIONS OF FOREIGN SOCIETIES.

### German.

SARCOMA OF TONSIL—PLACENTAL HEMATOMA IN THE DOG—OPERATIONS DURING PRIMARY ETHER NARCOSIS—LOCATION-SENSE IN THE SKIN.

THE German societies have been engaged with the following topics, many or all of which possess considerable merit.

VON HEINLETH, at the Aerztlicher Verein München, read a paper on "Sarcoma of the Tonsil." Three years ago a large tumor of this variety had been taken from the right tonsil, after the method of Krönlein. The patient is still without recurrence, and was therefore presented to the society as an example of permanent cure. About three months after the patient was first presented to the society, namely, about a year ago, a tumor appeared upon the opposite side. By the middle of August of that year the tonsil enlarged considerably and began to give symptoms. Upon examination on September 1, the tumor presented considerable size, a mass of hard consistency, a smooth surface, with a pale mucous membrane in contradistinction from the bluish-red color on the right side. There were no glands which could be distinguished as enlarged. The clinical diagnosis was confirmed by a microscopical examination; namely, sarcoma of the round-cell type. Inasmuch as the development of the tumor did not occur in or about the region of the first growth, it seems possible to consider this not a recurrence, but probably an independent neoplasm, due perhaps to a special predisposition on the part of the patient. The author could not be certain whether, after a long-standing right-sided pneumonia, a left-sided pneumonia appearing should be considered as a new disease or as a secondary manifestation, dependent upon the former. In his previous dissertation before the society he advanced the proposition that when the disease has progressed to considerable limits only the extensive extra-oral methods of operating, for example, those of Krönlein, Mikulicz, Brehn and others are available to produce any good results. If, however, early in the disease attempts are made at removal the intra-oral methods—for instance, that of Alexander Fraënkel—are advisable and available. In accordance with this principle, after a previous tying of the external carotid artery he removed the tumor, with a number of hard glands in close proximity to the blood-vessels. When the left side was operated on in this same manner, the wound healed promptly, and without any complications, which was not the case with the right side. Thus after 11 days the patient was discharged with a healed wound. Nine months have since passed without any signs of a return on the left side; therefore it is to be hoped that the patient will continue without any further trouble of this nature.

BONNET, at the Greifswalder medizinische Verein, June 7, 1902, read a paper on "Placental Hematoma in the Dog." The hyperemia of pregnancy in the mucous membrane of the uterus is to be considered as a nervous manifestation and continuation of the hyperemia of the menstruation. In this latter function there always is some bleeding into the mucous membrane and cavity of the uterus. Likewise, during pregnancy, similar bleeding may very well occur, and may vary apparently in localization and degree in different animals, frequently taking the form of intraplacental hemorrhages, appearing as a green or brown margin along this organ, or as a simple pocket of varying size. During the formation of the placenta not only are new vessels formed, but the old ones are elongated and enlarged. There is likewise the same process within the arteries and veins of the mucous membrane. They lose their muscularis, and become vessels with hardly any wall to speak of. Through retrogressive changes of the muscular coat, the motor elements of the circulation of the blood in this very much widened stream within the placenta are relegated to the muscular elements of the uterus and of the mesometrium. The general result of this is a manifest slowing of the total rapidity of the blood-current, even to a mild form of stasis and a moderate degree of edema, and occasionally greater or less bleeding into the placenta. These therefore frequently lead to the formation of a greenish color sometimes seen in the placenta, consisting chiefly of the coagulum which lies between the layers of the placenta and the choreon. The peculiar color is due to the unusual changes within the coloring matter of the blood, perhaps to hemachlorium, as described by Mickel. Small masses of hemoglobin and of coloring

matter are taken up by the epithelium of the chorion, and afterwards may be used by the embryo as a source of iron for its blood. These little hemorrhages might therefore be described as embryotrophic hematomata.

Ehrich, at the Rostocher Aerzteverein, July 12, 1902, read a paper on "The Advantages of Operating during the Primary Ether Narcosis." He described a procedure which has been used in his surgical clinics, especially in the Polyclinic, of operating during the first period of narcosis with ether. The method, which was originally described by Sudeck, rests upon the observation that after a few inhalations there is a temporary narcosis, during which in most patients little or no pain-sense is present, although the tactile sense is not interfered with. He regards this procedure as a worthy increase in the number of our methods of anesthetization, and deems its application suitable in those cases where ordinarily a local anesthesia would be desired, and where the production of deep anesthesia would hardly be justified. Up to the present time he has employed it for very brief operations like the opening of boils, the removal of carbuncles, extraction of teeth, reduction of fractures and application of painful dressings. Sudeck, however, has employed it for longer operations. The technic is exceedingly simple and demands no special practice. About 30 cubic cm. of ether are poured into a mask, preferably a Juillard, and after a few deep inhalations by the patient the cut may be made. If the respirations are not deep it is necessary to wait a little longer. The time necessary for it is surprisingly short, as is also the time for recovery, so that as soon as the dressing is applied the patient is normal again. Up to the present time, the dangers of deep narcosis in the slight operations have exceeded by far the dangers of the operations themselves; and this method is so simple and safe that it deserves universal adoption. After 60 experiments with it he has found only two individuals, and these nervous women, who became intoxicated with the ether after one or two inspirations; while on the other hand, in muscular men, the result was prompt and satisfactory. Although Sudeck regards the result as directly due to the action of the ether, Ehrich thinks that there is a psychical influence upon the patient as well, since the effects are decreased by suitable explanation and encouragement.

Von Frey, at the Physikalisch-medicinische Gesellschaft zu Würzburg, July 10, 1902, read a paper on "The Sense of Locality in the Skin." A previous communication by this author to the society as to the testing of this sense showed that not only one, but actually three organs are to be distinguished; namely, those respectively which appreciate simultaneous, successive and direct stimulation. The present paper was particularly concerned with the first of these three organs. The experiments were carried out by means of two electrical magnets, which placed two levers upon the skin at once. The result is that when two neighboring points are approached—that is, on the hairy parts of the body—two hairs could be distinguished only when they were 20 mm. apart, for example, on the forearm, and then only under the most favorable circumstances. The rule is to have the distances between them 100 mm. If two points are irritated at the same time the impressions seem to reinforce each other; that is to say, it is possible to find that by simultaneous stimulation an increase occurs in the sense. This increase is present also when the two points are so far removed from each other that it is possible to distinguish them separately. In cases where distinction between the two points is possible, in patients of refined sense, a curious fact is that the individual cannot tell whether the direction of the touch is lengthwise or crosswise of the limb.

## BYWAYS OF MEDICAL LITERATURE.—X.

### MEDICAL STUDENTS OF OTHER TIMES.

The medical student of the present day, who begins his medical studies under such excellent auspices in magnificent buildings where everything is provided for comfort and facility of education, can scarcely realize how great were the difficulties under which the medical students of only a few generations ago labored. There was even a prejudice against students of medicine among the populace, partly founded, perhaps, on the not altogether unjustifiable grounds that medical students were noted for more devil-may-care pranks than even the generality of students. Sometimes this feeling led to open rows in which more than blows of the hand were exchanged. Even fatal results were known to follow these quarrels.

When David Hosack, known to New Yorkers as one of the distinguished professors of medicine in the metropolis during the early part of the nineteenth century, and afterwards as a benefactor of the Academy of Medicine, began his medical studies, one of his first experiences was in such a row, more violent even than usual. His son, writing the biography of his father for Dr. Gross's Biographies of American Medical Men, says: "He had scarcely begun his studies before the celebrated 'Doctors' Mob' occurred, which threatened serious results to those concerned. It arose in consequence of the imprudence of some of the students carelessly pursuing dissection in the building upon the site since occupied by the New York hospital. This mob caused many of the professors to absent themselves from the city, and others to seek shelter in the city jail. Mr. Hosack, with the rest of the students interested, learning that the mob had seized upon and demolished the anatomical preparations found in the lecture-room * * * repaired immediately to Columbia College, with the view of saving such specimens as were to be found in that institution. Before reaching the college, however, and while on his way in Park Place, he was knocked down by a stone striking him on the head; he would in all probability have been killed had it not been for the protection he received from the neighbor of his father, Mr. Mount, who was passing at the time and took care of him."

Verily, medical student life in those days was something more than grind and cram for exams, with an occasional quiz and recitation to keep up the excitement.

### PLAYWRIGHT—EDITOR—PHYSICIAN.

The late Lord Tennyson's physician on the Isle of Wight is himself a literary personage of no mean celebrity. His name is G. H. R. Dabbs, and besides devoting himself to what is probably the busiest practice on the island, he sometimes drives 22 miles to see patients, and has the reputation of being very faithful in keeping professional engagements; yet he succeeds in finding time to write plays and an occasional novel, to act as member of the editorial staffs of two papers, and to drop into poetry when the muse inspires. Then he fills up his leisure with amateur theatricals. Not long ago a representative of a London paper wrote of him:

"When I dropped in on the doctor on a recent afternoon, he had just done his 40 miles, and written a three-column article *en route*.

'Well,' I said, 'you seem as fresh as paint, Doctor, but how you find time to carry on three or four professions as you do is a mystery.'

'There is no secret about it,' replied the cheerful doctor, who is as wiry as a barbed fence. 'I get up at four o'clock every morning, and utilize every moment of the day.'

'Four! How much sleep do you allow yourself?'

'Six hours. I have a desk in my bedroom, and from four to eight I write my plays, books, and articles; the rest of the day I devote exclusively to my professional practice.'

'The life of the country doctor in the Isle of Wight has always been a hard one. When I settled here there was only one miserable railway—the station at Newport, where I resided, resembled a wooden matchbox—and to fulfil my obligations I had to employ carrier pigeons. If I had six villages to visit, I took six pigeons with me in my carriage, and when I had finished the patients at one village I used to tie my prescriptions to a leg of a pigeon and toss the bird in the air. It at once flew home, where it was received by a man in the stable—a bell rang when it entered the loft—who, possessing himself of the prescriptions, took them to the chemist. The chemist then made up the medicines and sent them out by the carrier the same evening. I used pigeons as messengers for three or four years, when they were supplanted by the telephone and the telegraph. To-day things are different, of course, though a doctor in the island still has scant leisure. The distances are so great that one has to rely almost entirely on horseflesh as a means of getting about. I keep five horses, which is not one too many considering that I am often compelled to undertake journeys involving rounds of close upon 50 miles.'

'Then you must have had some exciting experiences.'

'I've broken 13 axles up to date, and sustained every kind of smash that can be conceived, from concussion of the brain down to a broken thumb.'

'How can you cross the island when the snow is on the ground?'

'We have very little snow in these parts. In 1881, however, we had a record fall. The snow was so deep that we were without letters for 14 days.'

'How did you carry on your practice?'

'I didn't carry it on. The people got well of their own accord.'

'It can't be very pleasant sitting in a carriage for four or five hours at a stretch.'

'You forget that I write large portions of my books while driving,' said the doctor."

In order to facilitate writing, avoid the drafts in his face, and at the same time escape the necessity for constantly saluting passers-by, Dr. Dabbs has had a specially planned carriage built for himself. His experience and the resultant invention may be of suggestive value to some of our country practitioners in the United States, so we give the London correspondent's account of them:

"A familiar spectacle in the island is the dashing by of a pair of spanking horses drawing a strange-looking carriage—a victoria with the hood reversed. Under the hood sits the doctor, perchance reviewing a book or scribbling off a bit of a play—economizing time as he rushes from patient to patient. The carriage, which is his own invention, was designed to enable him to get the maximum amount of air with the minimum amount of draft, and also to save his head-gear. Formerly, when he had an ordinary carriage and faced everybody he passed—he is known all over the island, of course—he had to raise his hat about a thousand times a day, the result being that he required a new hat every week; for, although the crown retained its pristine freshness, the brim, with the constant lifting, was reduced to a state of pulp. Now, however, with his back to the steeds, he is obscured from view, and weekly visits to his hatter are no longer necessary. The victoria is variously described, some of the irreverent natives calling it the 'coal-scuttle,' others the 'booby-hutch.'"

Dr. Dabbs does seem to be able to accomplish an enormous amount of work, and he enjoys excellent health, which he attributes to the open-air driving that his widespread practice compels him to take.

"Some idea of Dr. Dabbs's labors with the pen will be gathered from the fact that he is the proprietor of Vectis, a quarterly magazine, nearly every column of which he writes himself, and also of the Shanklin Gazette, to which journal he contributes five columns weekly. In addition he supplies the County Press with a weekly literary article. His latest play is 'The Dreamers,' and his latest book 'Ugly'—stories told by a hospital dog; and it is interesting to note that with the profits he derives from authorship he helps to maintain a cottage hospital. There is probably no harder-worked man in England than this popular medico. 'The most punishing spell of labor I ever performed,' he remarked in reply to a question, 'was this. When a patient of mine was dying at Hampstead he expressed a wish to see me once every 24 hours, and I managed it in this way: I worked all day long in Shanklin, and left by the 8.40 P.M. mail to London; reaching Waterloo at 3.40 A.M., I drove to Hampstead, and after spending an hour and a half with my patient I hurried to Waterloo, and catching the 7 A.M. train, I was back here for my patients at 11 A.M. This I did for three weeks.'"

### MENTAL AND MORAL HEREDITY IN ROYALTY.

Dr. Frederic Adams Woods of Harvard University has had a very informing series of papers on this subject in the August, September and October numbers of the Popular Science Monthly. The English Royal family, the Stuarts, the Hohenzollerns and the Hapsburgs have all been followed in their pictures for many generations, and in the histories of their individual careers. Some of the material thus deduced is very suggestive for those who are interested in the heredity of dispositions as well as of peculiar features.

One of the most striking passages in the series of essays is that which is concerned with the Hapsburg lip. A series of illustrations are given in which the great swollen, protruding lip of the Hapsburgs is exhibited in many generations. Altogether it seems that in various degrees of intensity this undesirable feature can be traced through no less than 18 generations of the Hapsburg family, making its appearance in at least 41 of the various descendants. It is first recorded in history as occurring in Zymburga, who was born in the latter part of the fourteenth century and became the wife of Ernest, the second Patriarch of the house of Hapsburg. In its latest manifestations it appears at the present day, though with somewhat diminished force and modified form, in the young King of Spain. This is a remarkable instance of the course of heredity in perpetuating a physical trait, and is often quoted as an instance of prepotency, the male line being able to transmit a deeply rooted though comparatively unimportant peculiarity without the features from the maternal side having any influence in counteracting it. It is a very curious reflection that this large ugly lip was coincident in most generations with the neurosis which characterized the House of Hapsburg in many generations. It is curious, too, that occasionally the peculiarity has jumped a generation and then reappeared in characteristic form. In the more recent generations it seems to be less frequent than formerly, and therefore appears to be running out of the stock. A study of the charts of descent shows that it very frequently happened that those chosen by fortune to be the progenitors of the head of the house in successive generations possessed this special peculiarity to a marked degree. Coincidence then would seem to have something to do with the preservation of the remarkable feature.

The whole question shows the importance of the in-

fluence of intermarriage. Recent rumors with regard to the young King of Spain would seem to indicate that he possesses some of the peculiar ways and uncontrollable habits of his Hapsburg relative, the late Crown Prince Rudolph of Austria. The young King's mother, through an Austrian archduchess, seems to be an eminently sensible little woman, and yet the mental peculiarities of the Austrian blood are coming out in the next generation. Observations along these lines are mainly in the hands of physicians, and it is unfortunate for biological science that more of them are not regularly tabulated by family physicians, especially when several generations of physicians occur in the same family.

PREPOTENCY IN POLYDACTYLOUS CATS.

It does not seem exactly respectful to discuss the inheritance of a superfluity of toes in cats just after reviewing the question of the inheritance of peculiarities in royal families. But nature and biology have these democratic juxtapositions, and we must put the blame on them. Mr. Harry Beal Torrey of the Zoological Laboratory of the University of California has been studying a series of cats in the possession of a Los Angeles family, many of which are furnished with an abnormal number of toes on both fore and hind feet. All are descended from a stray female of unknown pedigree, which possessed 22 toes, six instead of five on each fore foot, and five instead of four on each hind foot.

This female, crossing with normal males, has always perpetuated her peculiarity to a certain extent. In one litter one of the kittens had 20 toes, instead of the usual 18. In another two of the kittens had over 20 toes. Mr. Torrey has had under observation a female of the third generation from this cat, most of whose progeny have more toes than normal. One of the kittens has 25 toes, two have 24, one of them having seven toes on each fore foot, and more than 50 per cent. of descendants are abnormal in their number of toes. It seems clear that the total number, as well as the number on each fore and hind foot, is increasing from generation to generation.

It is well known that tendencies to the possession of six fingers and six toes in human beings are distinctly hereditary. One family of six-toed individuals has been traced through four generations. In human beings it has been noted that these peculiarities are more liable to follow the female than the male side of the house. In Mr. Torrey's observation there is a very curious and interesting feature in this respect. There seems to be a very distinct and extremely remarkable prepotency of sex. The male cat with 25 toes, when crossed with normal females, had no influence on the number of toes in the offspring so far as information could be obtained. This result is all the more surprising because in three generations the females have actually acquired the power of transmitting superfluous toes in even greater number and to more and more of their offspring. This subject is, of course, an extremely interesting one from a biological standpoint, and it suggests some of the possibilities of observation on domestic animals that are constantly opened to those who have eyes to see.

GRATUITOUS MEDICAL SCIENCE.

A young man who writes a novel or two and shows his ability to sling the King's English in essay form is sometimes asked to write a column for a weekly paper. As sure as fate, when things political and literary are dull, he will feel himself called upon to write medical science (save the mark!) for the many. Oh, the poor many, how sincerely they would have to be pitied only that they do not take all the medical advice thrust upon them! The last offense of this kind turns up in a recent Sunday issue of the New York Times, in the department called "The Looker-On." Usually the Times is not guilty of indiscretions of this kind, which makes the present offense all the more glaring. Consider this as a serious contribution to progressive medical science: "Another article of diet, famed in song and story and now falling into merited disrepute, is bread and milk. Milk is about the most dangerous of the undeniably wholesome foods. It cannot be taken with a certainty of good results unless it is taken absolutely alone and has a chance completely to disappear from the stomach before anything else is eaten or drunk. Bread and milk in combination is not a food. It is at best a burden, at worst a poison. To feed it to children, as all mothers used to do and as some mothers still do, is to assail their health at its vital point.

"The worst thing about improper food and drink is that it, like the protective tariff, does its damage usually in a place remote from its point of initial contact. You eat or drink something you ought not; you persist in doing it; you fall ill; the doctor comes and finds that you have rheumatism or pneumonia or typhoid fever. And it never occurs to him or to you that the real reason for your illness is that you have weakened the resisting power of your whole system by what you have put into your stomach."

There was a time when everyone who wrote at all thought he could write a pretty theory about electricity and the beauties of chemistry, but that sort of thing has fortunately gone out of fashion with the real progress of science, and theorizing is left to scientists. Let us hope that the same respect for medicine will soon come to be the order of the day.

## SOCIETY PROCEEDINGS.

### ACADEMY OF SURGERY OF PHILADELPHIA.

*Stated Meeting, Held October 6, 1902.*

The President, Richard H. Harte, in the Chair.

**Falls Upon the Buttocks.**—Dr. Oscar H. Allis said that in some cases of falling upon the buttocks there was immediate helplessness, with severe pain upon movement, while in others the patient was fairly comfortable from the start and finally able to move about with more or less facility. He spoke briefly of four points: (1) Cases followed by helplessness; (2) cases followed by recovery; (3) pathological conditions found in cases coming to autopsy; (4) operative treatment. Under the first head Dr. Allis gave brief notes of three cases in which falls were followed by symptoms of fracture of the neck of the femur. No attempt was made to effect cure in these patients, they being made as comfortable as possible. All remained helpless during the rest of their lives, from four to six years. To show that these results were not the fault of the treatment, three similar cases were detailed under the second point. The injury and signs of fracture were the same as in the first three cases, but the results in each were different in that each patient was afterwards able to walk and had a fairly useful joint. No particular attention was paid to the thigh, as in the first series, the only efforts being to make the patient comfortable and avoid the presence of pressure-sores. As possible explanations for this disparity of results in apparently similar cases, Dr. Allis suggests: (1) The springing up of osteophytes, which was proven to be true in Case I, from which specimen was shown; (2) the fall may produce concussion of the joint, a

mild subacute arthritis following, areas of absorbed cartilage with denuded bone being present; (3) the sciatic nerve may be caught, though Dr. Allis knows of no evidence to prove this; (4) the ligamentum teres may be torn, although there is no basis for a positive statement as to this condition. As to treatment there is little to offer. If operation is done it should be when indicated by the persistence of pain for more than one or two months. If the patient's age and strength permit of this procedure it is probably the best treatment and is justifiable.

Dr. R. G. Le Conte said that one case under his observation would help bear out the statements made by Dr. Allis. The patient was a woman who one year before had fractured the neck of the right femur. Since that time she had been helpless and in great pain. She had also suffered for years from rheumatic gout or arthritis deformans. Ten months after the injury was received Dr. Le Conte operated with the view of freshening the ends of the bone and inserting a peg. He found that the neck of the bone had been almost entirely absorbed and the head had areas of eroded surface. In view of the condition present and the helplessness of the patient the head of the bone was excised. At the end of six weeks the patient was about on crutches. She is comparatively comfortable, except that the knee of the same side is exceedingly painful from the other condition named. The pain in the hip was entirely relieved by the operation. It is a question if operation in these cases is of much benefit as regards locomotion.

Dr. R. H. Harte said the subject under discussion was of great interest to every surgeon. Cases of intracapsular fracture do run different courses as portrayed by Dr. Allis. For this there must be some definite cause. The diagnosis is reasonably easy, being made from the ordinary symptoms of shortening, eversion, etc., and is undoubtedly correct in both classes of cases. The routine treatment by rest, extension and immobilization is also the same in all. Yet in some cases the patients are comfortable, while in others they scream with pain whenever the leg is extended. Dr. Harte explains our ignorance as to why such different results follow by saying that we cannot tell what takes place in the joint at the time of injury. In some the bone simply breaks straight across, while in others it is comminuted. This may cause perforation of the joint or irritation of neighboring tissues by a spicule of bone. In all cases there is induced a greater or less degree of arthritis. This is accompanied by pain, as when it affects the wrist or other joints, and is probably one of the greatest reasons for pain in some of these cases. As to treatment, operation is justified if pain and helplessness persist after a certain length of time. This consists in resection of the head of the bone. In this class of patients there is probably more danger from the anesthetic than from the operation itself.

Dr. W. J. Taylor considers the pain in these cases as largely due to arthritis. He lately had charge of an old lady of eighty-two years who received an impacted fracture of the neck of the femur with 2½ inches shortening. A skiagraph showed the presence of a spicule of bone near the fracture, but there was no evidence as to whence it had been derived. This patient had at no time any pain whatever. She was kept in bed three weeks with light extension upon the leg. She is now able to walk about and even to go up and down stairs. There was evidently no true arthritis in this case.

Dr. G. G. Ross mentioned the case of an old lady near his home who sustained an intracapsular fracture of the femur when she was one hundred and two years of age. She recovered and was able to walk, and lived until the age of one hundred and six years.

In closing, Dr. Allis said he would like an explanation of where the osteophytes came from in the specimen he exhibited. Dr. Harte said they may have come from the periosteum of one side which had not been destroyed.

**Amputation of a Leg Under Intraneural Anesthesia.**—Dr. John H. Gibbon reported this case. The patient was a man of fifty years who had a tuberculous ankle-joint. After examination it was decided that efforts to save the joint would be useless, but the man was told that incision into the joint was to be made as a last resort for confirming this opinion. The sciatic nerve was then bared under local anesthesia and No. 1 Schleich's fluid injected into it. The same process was then used on the anterior crural nerve. It was thought that anesthesia would be immediate. It was not, and after waiting four or five minutes chloroform was sent for. Before it was used, however, the man said he felt a queer sensation in the leg, and it was found that sensibility was diminishing. An incision was then made and the diagnosis confirmed. The patient felt this, but said it did not hurt. While an attendant engaged him in conversation a circular cuff was made and the leg amputated. When the patient heard the saw he said, "He is not taking off the leg now, is he?" His question was parried, and he did not know that the leg had been removed until he was in the ward. Regarding the question of shock, the temperature was never below normal, and the respirations only increased two per minute. The pulse rose from 64 to 112, Dr. Gibbon explaining this by the fact that through faulty technic the exposure of the sciatic nerve was prolonged and caused some slight pain. No pain was felt while the anterior crural was being exposed. The injections, after exposure of the nerves, were made paraneurally and intraneurally. The wounds healed promptly, and the patient was out of the hospital in less than one month.

Dr. R. G. Le Conte, who was present at the operation, said he could confirm Dr. Gibbon's statement that the man suffered no pain during the amputation. He thought a very probable explanation of the rise in pulse-rate was that a perceptible quantity of cocaine was used and absorbed. He mentioned the case of a man from whose scalp he removed a wart after injecting a two or four per cent. solution of cocaine. Exhilaration followed, and when the patient soon afterwards joined a party of friends to go on a coaching trip they all thought him to be drunk. Therefore, Dr. Le Conte thinks the quickened pulse in the case under discussion was due to cocaine and not to any nervous phenomenon.

Dr. J. K. Young asked if there was any danger to the integrity of the nerve in the use of this method.

In closing, Dr. Gibbon said that exhilaration was one of the first effects of the use of cocaine, and he had had a case similar to the one related by Dr. Le Conte. He had then used a four per cent. solution, however, and did not think that a solution of one-fifth of one per cent. would have this effect, although it might when injected into the nerve itself. The patient had shown no exhilaration after the injection. In answer to Dr. Young's question he said that Drs. Crile and Matas had noticed no untoward effect upon nerves after injection, and there was no evidence of it in his case while he was under observation.

**Gall-stones in the Common Duct.**—Dr. Robert G. Le Conte reported an interesting case. The patient was a man of thirty-four years, who during four months had six attacks of abdominal pain, nausea, vomiting and jaundice, and had lost 30 to 40 pounds in weight. When he entered the hospital he had a

leucocyte count of 11,900. Under the influence of rest, light diet and sodium phosphate his condition improved and he left the hospital, but only to be readmitted later during another attack. The leucocytes then numbered 10,200. Operation revealed a small thickened gall-bladder containing 200 to 300 stones. There were also some in the cystic duct and two in the common duct. By manipulation one was pushed out through the gall-bladder, but an incision into the duct had to be made to free the other. The opening in the duct was then partly closed by one catgut suture, a gauze drain inserted, and a tube drain inserted in the gall-bladder. The former was removed after 48 hours, the latter four days later. Recovery was uneventful. The small sinus which remained became infected after the patient left the hospital, but healed under appropriate treatment. At this time the patient said he often vomited about midnight, there being no nausea. Two points in this case were considered of interest: (1) The closing of the common duct by suture. Le Conte advocates doing this when it is possible. When the duct is thickened, friable, and difficult of access he would not attempt suture, as it will probably close itself. (2) Should all the adhesions encountered in such a case be broken up? When the bile is sterile it probably makes no particular difference how this question is answered. But when there is a possibly infected bile and adhesions are present around the gall-bladder, pylorus, duodenum, etc., only enough should be broken up to allow the operator a sufficient field to work in, as they help in limiting infection if it occurs. It is probable that some of these adhesions caused the curious vomiting mentioned as occurring six weeks after operation. It is thought, however, that they will stretch and cause no further trouble.

In the discussion Dr. Allis said that the question of suturing the duct was a very pertinent one. There is danger of infecting the site of operation by passing through the mucous membrane, even if a very small needle and fine catgut be used. If the duct is thickened the incision will be held in place by packing. Finally, if a part of the incision is left open, all of it should be left open.

Dr. J. H. Gibbon, during the course of his remarks on this subject, exhibited a large and greatly thickened gall-bladder which was removed from a patient a few days previous. The bladder was the seat of beginning gangrene as the result of a large stone which had been impacted in the opening of the cystic duct. The patient's temperature was 102° F., and there was pain but no prominent symptom of obstruction. Rigidity was marked. The leucocyte count was 37,000, a point which helped lead to diagnosis of gall-bladder infection, as the highest count the writer has seen in appendicitis is 33,000. Operation revealed a gall-bladder full of stinking pus. The speaker called attention to the similarity between gall-bladder disease and appendicitis. The organ had the same appearance as a diseased appendix; the colon was injected; the omentum was anchored over the seat of inflammation. An attempt to ligate the cystic duct was made, but the bladder pulled loose during the effort. The cystic duct bled furiously and was too rotten to hold forceps. It was packed with gauze. The patient was showing signs of recovery. The leucocytes dropped to 12,800 but again rose to 20,000. This was thought to be due to reparative processes.

Dr. W. L. Rodman said that Dr. Le Conte's case was an interesting one. He thinks that the question of suturing the common duct was pretty well settled by Fenger, who demonstrated that it need not be closed in all instances. Closure is not necessary so long as the bile is aseptic. Suture of the common duct is one of the most difficult tasks encountered by the surgeon. Lately he has seen Mr. Robson operate and suture the duct with great facility. This was brought about by an incision in the right semilunar line, curved somewhat at the upper end. With a bag placed under the patient's back, the liver and gall-bladder were brought into the field of operation in a most perfect manner, and the common duct was comparatively easy of access.

**Intestinal Obstruction.**—Dr. W. T. Taylor reported a case of intestinal obstruction due to Meckel's diverticulum and appendicitis. The patient was a female of twenty years, who had had no bowel movement for six days, and had fecal vomiting. There had been a similar attack one year before. There was no special abdominal distention. The omentum was found adherent to the bladder and appendix. There were many adhesions of the appendix, but no evidence of present trouble in that organ. The adhesions apparently accounted for the obstruction. Search, however, revealed at one point distention of the small intestine, and obstruction due to a remnant of Meckel's diverticulum was found. At a distance of 32 inches from the cecum was a single fibrous band, one-eighth inch in diameter and having no lumen, which united two loops of intestine, passing through the mesentery. There had evidently been constriction for a long time, but strangulation was recent.

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## SOCIETY OF ALUMNI OF BELLEVUE HOSPITAL.

*Meeting of October 1, 1902.*

The President, Dr. Robert T. Morris, in the Chair.

Dr. Alexander Lambert, the retiring President, introduced the President elect, Dr. Robert T. Morris, with a few well-chosen words.

**President's Address.**—Dr. Morris said that as 20 years ago he left Bellevue Hospital he felt disposed at this time to be retrospective. Among the changes noted in that time was the great advance made in the administration of anesthetics by special anesthetists, and the introduction of cocaine for local anesthesia. At the beginning of the period referred to organotherapy had not been thought of, and the X-ray was, of course, not known. In the old days at the hospital there were only one or two men on the staff who believed in antiseptics, and when one of their number, thoroughly trained in Germany, began the practice of antiseptic surgery he was ridiculed by the others. In those days at the medical society meetings it was the custom to listen to the papers with great show of respect and to refrain from public unfavorable criticism, although much of the latter was indulged in afterwards in private. Fortunately in more recent years the tendency had been to discuss scientific contributions vigorously and in a straightforward manner, though impersonally.

The specialists of that day were chiefly practitioners confining their practice to diseases of the eye, ear, nose and throat. Gynecology was only just beginning to be recognized as a specialty. A few years later it became a marked specialty, and still more recently reverted back to surgery. On the other hand, orthopedic surgery had branched off more and more from general surgery. The rapid evolution of specialties had necessarily led many to become specialists without being properly equipped therefor.

Concerning the moral right of those in general practice to undertake special work when there were many specialists at hand, the speaker said that this was a complicated subject, but the statistics available showed that, in certain lines at least, such practice had no moral justification. For example, a surgeon in a neighboring State, who boasted that many practitioners in that State were not afraid to do abdominal operations, had

reported from these sources 163 abdominal operations, with 102 recoveries and 61 deaths! This large death-rate was contrasted by the speaker with the three to seven per cent. of deaths reported by experienced operators in that field. Dr. Morris thought no general practitioner had a moral right to do such practice unless with the deliberate intention of devoting himself to special work.

Reference was then made to the modern tendency in the profession to commercialism. He thought many physicians were too modest in their demands for remuneration, and insisted that if large fees were demanded and the work done made at the same time of proportionate value, the public would be quick to appreciate this and respond accordingly. The public did not appreciate the motives prompting the charging of small fees, and were disposed to look upon it merely as a weakness. While specialists filled a most important sphere, the general practitioner must always be as necessary, and must be thoroughly trained and educated, so that when special skill was required he would be "the one who knows who knows." The charging of large fees, the rendering of bills at stated intervals and insisting upon their prompt payment, if need be by legal process, he believed to be thoroughly professional and right. The laborer was worthy of his hire; moreover, many of the experienced and charming physicians of the older school who looked askance upon this commercial tendency were the very ones who, having been deprived for years of their rightful compensation, were not in the position at the present time to pay for special apparatus and special skilled assistance such as they should have in order to properly carry on the modern practice of medicine. It was another matter, however, to indulge in the practice that had recently grown up in the West, *i. e.*, the division of fees between specialists and the physicians referring cases to them. There was only one word which properly described this, and that was "collusion." If, however, the fees were divided with the knowledge of the patient it was entirely different. This practice of dividing fees would never appeal to the best men.

It was reassuring to note that there had been in recent years no increasing tendency to advertise, even though one could be assured of a speedy competence by advertising in the daily press and living up to the claims made. There was a distinct tendency at the present day for the public to patronize those physicians who were most scientific and most thoroughly equipped for their work. There was a better *esprit de corps* noticeable in the medical profession, and a society like that of the alumni of Bellevue Hospital was a potent factor in fostering this spirit. This tendency had led to the presentation before this society almost uniformly of papers of high scientific character, and had elicited fair scientific criticism of these contributions.

**Volvulus as a Cause of Intestinal Obstruction, with Report of Three Cases Successfully Operated Upon.**—Dr. John F. Erdmann presented a paper on this subject. He quoted the article of Dr. C. L. Gibson with regard to the frequency of volvulus as a cause of intestinal obstruction, the relative frequency in the two sexes and the results of operation. Volvulus usually occurred in mature life, the average age being forty-five years. Shock was not usually evident in volvulus until late, and often two or more days would be consumed in making the diagnosis. The onset was usually indicated by pain. If defecation were possible the part of the bowel below the volvulus might be expelled. The treatment was generally operative, although in recent years some results had been secured by placing the patient on one side for a time and then having him roll suddenly to the other side. The difficulties of this method were obvious. If on opening the abdomen volvulus were present, there would be found such enormous distention of the intestine as to necessitate the employment of some means for securing the escape of the gas. This was generally best accomplished by the use of the rectal tube. In his first case, after this had been done, anchoring sutures were taken in three situations. He did not believe that plicating the mesentery was of benefit in preventing recurrence. He did not believe that with the atonic overdistended sigmoid primary resection was a good means of preventing recurrence; it should be left for a secondary operation.

*Case I.*—The patient was a male, forty-three years of age, first seen in consultation in July 28, 1899, four days after the onset of abdominal pain. Various purgatives had been given without any result. The man's temperature was 99.5° F. He was at once removed to hospital with a diagnosis of volvulus. A very long incision was necessary because of the great distention. The twist was from left to right, and was situated opposite the fourth lumbar vertebra. Considerable difficulty was experienced in reducing the twist, but after this had been accomplished a rectal tube was inserted and the gas expelled by manipulation. The abdomen was closed without a drain. On the two following days there were numerous passages from the bowel. August 13 the patient was discharged "cured."

*Case II.*—This patient was a woman of forty-one years, with a strangulated ventral hernia. The bowels had been absolutely constipated for three days and there was constant vomiting. The pulse was 76 and the temperature 100° F. Owing to the bad condition of the patient the operation was done under spinal anesthesia. Two loops were found, one of which was gangrenous and twisted upon itself from left to right. It was held by a band, which was untwisted and resected without the patient's experiencing any pain. On the tenth day she suddenly went into collapse, but was resuscitated and thereafter made an uneventful recovery. The distention following the volvulus was the cause of the strangulation of the ventral hernia.

*Case III.*—The third patient was a male who, when first seen, was in a state of mild shock. A twist of 180° of the sigmoid from left to right was found. There was no great distention, and the twist was easily reduced. Some fluid was found in the peritoneal cavity, and inquiry elicited a history of tuberculosis. On the ninth day the wound suddenly broke open on coughing, and a coil of intestine, six inches long, protruded between the recti. This was reduced and the wound again coaptated. After this recovery was rapid and uneventful.

Discussion.—Dr. C. C. Barrows said that he had had no personal experience with volvulus, and had been under the impression that it was a much rarer condition. He was particularly interested in the case in which the volvulus existed within the sac of a reducible hernia. He thought this might readily occur where the hernia was manipulated by the person in the effort to reduce the hernia from time to time. Dr. Erdmann was to be congratulated on the successful issue in these cases.

Dr. William J. Chandler of South Orange said that he had had a number of cases of volvulus, but in most of them the duration of the volvulus had been so great that a bad result was to be expected.

Dr. Brown said that in a case of volvulus which he had seen, after various other measures had been tried without avail a siphon of Vichy was brought into requisition, and injected into the rectum, with the result that the volvulus was quickly reduced.

Dr. Robert T. Morris said that these patients failed very fast because of a saprophyte intoxication from the bowel. He had employed intravenous saline infusion at the outset, before operating, in order to raise the

vascular tension and secure the elimination of these saprophytic toxins. This procedure, when done before the operation, greatly stimulated the patient, and placed him in far better condition for operation. A method that had been employed some years ago consisted in suturing the volvulus to the abdominal wall after straightening the loop. This method of Roser was intended to prevent recurrence, but it seemed to him that there was quite as much danger of recurrence because of the enormous distention of the bowel. The introduction of water or gas into the bowel had been employed quite extensively, and with varying results. The cases should be carefully selected for this treatment, and it should only be tried when the patient had been prepared for an abdominal operation. In most cases the method was dangerous because at the point of angulation there was apt to be ulceration or gangrene, or still more commonly, a fragility of the bowel arising from the presence of serous infiltrates. This seemed to him an exceedingly important point.

Dr. Alexander Lambert said that Hemmeter gave, in his book, the proportion of volvulus causing intestinal obstruction as 19 in 1,000 cases, and it was there spoken of as the rarest form of intestinal obstruction.

Dr. Erdmann, in closing the discussion, said that volvulus was found quite frequently in herniæ, but ordinarily it was not sufficient in degree to demand surgical interference. He was inclined to think that many of the cases reported by Dr. Gibson were examples of volvulus within the hernial sac. He recalled having seen two cases at the Gouverneur Hospital, one in a hernia. The toxemia, referred to by Dr. Morris, was usually very evident, and it was for this reason that he had introduced the rectal tube in cases of volvulus of the large bowel. The fragility of the bowel at the point of angulation, as a result of serous infiltration, was also very noticeable in intussusception. If such a condition had been present in Dr. Brown's case the result of the injection would have been a rupture of the bowel and death.

## BOOK REVIEWS.

A Brief of Necroscopy and Its Medico-Legal Relations. By Gustav Schmitt, M.D. Funk & Wagnalls Company, New York and London.

This little volume will make a very handy reference book for coroners' physicians and the medical men who have to make autopsies for medico-legal purposes. It is a wonderfully complete compendium of many items of information that are most desirable and that often have to be sought in larger works at great expenditure of time. The brief deserves a place in the library of lawyers as well as physicians, and will be useful to the expert witness who wishes to be prepared for the ordeal.

Cellular Toxins, or the Chemical Factors in the Causation of Disease. By Victor C. Vaughan, M.D., LL.D., Professor of Hygiene and Physiological Chemistry and Director of the Hygienic Laboratory in the University of Michigan, and Frederick G. Novy, M.D., Sc.D., Junior Professor of Hygiene and Physiological Chemistry in the University of Michigan. Fourth edition. Revised and enlarged. Lea Brothers & Company, New York and Philadelphia.

The old familiar work on ptomaines and leucomaines has been so thoroughly revised, rearranged and rewritten that it appears in this the fourth edition under an entirely new name.

It is an entirely new book, and one that breathes the spirit of modern investigation from cover to cover, yet couched in the senior author's inimitable style in such simple and practical language that an otherwise difficult and technical subject is made attractive and profitable to the practising physician as well as to the laboratory worker.

Inasmuch as the work is practically a new one, a brief recapitulation of its contents is here given. The four opening chapters discuss the subject of bacteria, bacterial diseases, the chemical products of bacteria, an historical sketch of the bacterial poisons and the bacterial poisons of some of the infectious diseases.

Chapters v, vi, vii, viii and ix take up some of the problems of defense against the poisons discussed, particularly dealing with the germicidal properties of the blood-serums, the alexins, precipitins, lysins, bacteriolysis and the agglutinins, thus leading up to the large subject of immunity, which is discussed from its various sides.

Food-poisoning is fully elaborated in the following two chapters. Nowhere in the English language can there be found so full and so authoritative an exposition as here.

The remaining four chapters deal with more strictly chemical problems which are coming to be regarded as most necessary of solution if any advance is to be made in the study of the complicated changes of disordered metabolism.

From all standpoints this work is to be most heartily commended.

Typhoid Fever. By J. T. Moore, M.D., M.C.P.S., Professor of Theory and Practice of Medicine, Medical Department of Hamline University, Minneapolis, Minn. G. P. Engelhard & Co., Chicago.

This is one of the Standard Monograph Series, and is issued most opportunely for the season when typhoid fever is most frequent. It contains in brief compass all that is important and practical in our present-day knowledge of typhoid fever and is especially complete in the chapters on diagnosis and treatment. The discussion of the Widal test is very thorough and the exact limitations of the diazo reaction are well told.

Transactions of the American Climatological Association. Vol. xvii, for the year 1901.

For a number of years this association has been doing an appreciable amount of very excellent work, and the material here recorded for permanent use constitutes a praiseworthy memorial to the members of this numerically small body of workers.

Climatological papers on Porto Rico, Augusta, Ga., Newport, R. I., Nantucket, New England and Southern California are contributed by Drs. Alden, Coleman, Rives, Williams, Hinsdale, Fisk, and Budge respectively.

The large number of papers on tuberculosis here assembled makes a formidable array of authority.

Gout, nervous disorders and cardiac diseases are also treated of by various writers.

La Guerison de la Morphinomanie sans Souffrance. Par Dr. Oscar Jennings. A. Maloine, Paris.

This is a French translation of Jennings's small monograph on the treatment of the morphine habit.

For a number of years this author has worked conscientiously for the alleviation of this constantly growing class of unfortunates, and his crystallized experience is worth much.

That the average practitioner regards the question of treatment of the various forms of the opium habit in a markedly pessimistic light is not to be wondered at. The task is a monumental one, and for most patients it does not seem worth while. Jennings has elaborated

a system founded on practical lines, and much can be gained from his work. He is an advocate of the tapering-off method which many authors condemn. It must be confessed that these latter usually show by their writings a very slight acquaintance with the feelings of their patients. The treatment by "souffrance," as advocated by Jennings, has a great deal to recommend it.

DIE FREIHEIT DES WILLENS VOM STANDPUNKTE DER PSYCHOPATHOLOGIE. Von Prof. Dr. A. HOCHE in Strassburg. J. F. Bergmann, Wiesbaden.

THE discussion of the freedom of the will from the standpoint of psychopathology is certainly a "large order," yet the author has been able to shed some light on the subject, and has given withal a very readable essay which makes a welcome addition to an excellent series, the "Grenzfragen des Nerven und Seelenlebens."

THE STUDY OF THE PULSE; ARTERIAL, VENOUS, AND HEPATIC, AND THE MOVEMENTS OF THE HEART. By JAMES MACKENZIE, M.D. (Edin.) Burnley. The Macmillan Company, New York.

FOR English readers at least, perhaps no other school of investigators has done so much and so well in the study of diseases of the circulatory system as the Edinburgh school. This study is one of the best of its kind.

Begun, some 20 years ago, as the author says in his preface, originally to ascertain the changes in the maternal circulation during pregnancy, the inquiry has broadened out so that it embraced all forms of heart-failure.

As the author has pointed out, our present-day knowledge of the clinical significance of pulse irregularity is not merely imperfect, it is chaotic; and he has most successfully brought a certain amount of orderly information from the confusion.

In the earlier chapters are discussed the determination of the value of symptoms, instrumental methods of examination employed in the research, and interpretation of a sphygmogram.

The author is not one who would relegate the sphygmograph to the physiological laboratory, for he holds that it may be made a most valuable instrument for clinical study, that whereas much that was claimed for it in the days of its introduction has been shown to be illusory, yet rightly interpreted it will yield results of fundamental significance.

Chapter IV, on the movements of the heart in health and in disease, is a masterly summary of a wide topic. Two chapters follow on the pulse; one on examination of the peripheral circulation, and one on arterial pressure. Chapters IX and X discuss pulse irregularity, and, the following four chapters treat separately upon different forms of irregularity, increased frequency, diminished frequency, the pulse in febrile conditions, some characteristic pulses and the relation of the pulse and the respiration.

Part II opens up almost a new field, the pulsation in the veins and liver. The author here presents a veritable mine of useful clinical information regarding the activities of the different chambers of the heart, particularly the auricles. Constitution of the venous and liver pulses, Conditions giving rise to the various forms of the venous and liver pulses, The auricular form of the venous pulse, Paralysis of the auricle and the ventricular form of the venous pulse, Enlargement and pulsation of the liver, The clinical significance of the venous and liver pulses—these are the chapter headings in this fascinating part of the book.

Part III deals with the venous and liver pulses in irregular heart-action.

A certain lack of coherence in the plan of the work, an unavoidable blemish, as the author himself recognizes and deplores, is the only marring mote in this most excellent treatise. The work will repay serious and careful study, and will unquestionably do much to enlighten the busy practitioner in his daily round of duty.

TRANSACTIONS OF THE AMERICAN MICROSCOPICAL SOCIETY. Edited by the Secretary, HENRY B. WARD. Vol. XXIII. Twenty-fourth Annual Meeting, held in Denver, Colorado, August 29, 30 and 31, 1901.

THE annual reports of this society have always proved most interesting and acceptable. The present volume is no exception to the rule.

While the subjects discussed this year are further from the practical field of medicine than those of 1900, yet a few are of importance in the zoological and botanical domains.

An interesting study in embryology, "The Solution of the Eel Question," by C. H. Eigenmann, outlines the development of our knowledge on this subject. How, when and where eels reproduce has been till within recent years unknown. Aristotle first propounded the question, and from the discoveries of Scopoli in 1777 to the time of Grassi in 1897 facts bearing on the problem have been turned up. At the present time it is known that eels, both male and female, migrate to the ocean during October to January; that these eels probably deposit eggs that are found on the surface of the ocean during the following August to January; that the eels do not ripen in shallow water, but the female at a depth of at least 560 yards; that the eel has a metamorphic stage, and that the young eels enter the streams during spring about two years after their parents entered the sea.

Dr. W. C. Krauss of Buffalo contributes an appreciative sketch of the lives of the Spencers, a family that stands high in the annals of American microscopy.

D. D. Jackson describes a new Crenothrix from water, a related species to the Crenothix kühniana which caused so much difficulty with the Berlin water-supply in 1878.

Geo. C. Whipple and H. N. Barker contribute an interesting paper for those working on the problems of potable waters. It treats of the relation of dissolved gases to microscopic life.

The Curvipes or water-mites, an interesting group to the microscopist, is well handled by Robert H. Wolcott. His paper is richly illustrated, and analytical tables for the species are worked out with elaboration.

THE MEDICAL DIRECTORY OF 1902.

THE Medical Directory of New York, New Jersey and Connecticut for 1902 has made its appearance neatly and attractively bound, and full of valuable information for every doctor in any one of the three States. The book is published by the New York State Medical Association. The lists of physicians have been sifted and amplified by careful comparison with certified lists from registers of the county clerks' offices, so that no trouble or expense has been spared by the committee of publication to make every statement reliable. The total number of names contained in the lists of physicians is 13,364, of which 10,606 are in the State of New York, 1,655 in New Jersey, and 1,103 in Connecticut. Of the 10,606 names in the New York State lists, 3,948 are credited to the Boroughs of Manhattan and Bronx, 1,323 to the Borough of Brooklyn, 115 to the Borough of Queens, and 58 to the Borough of Richmond, a total for Greater New York of 5,444, which leaves the number of physicians residing in the rest of the State outside of this territory 5,162.